

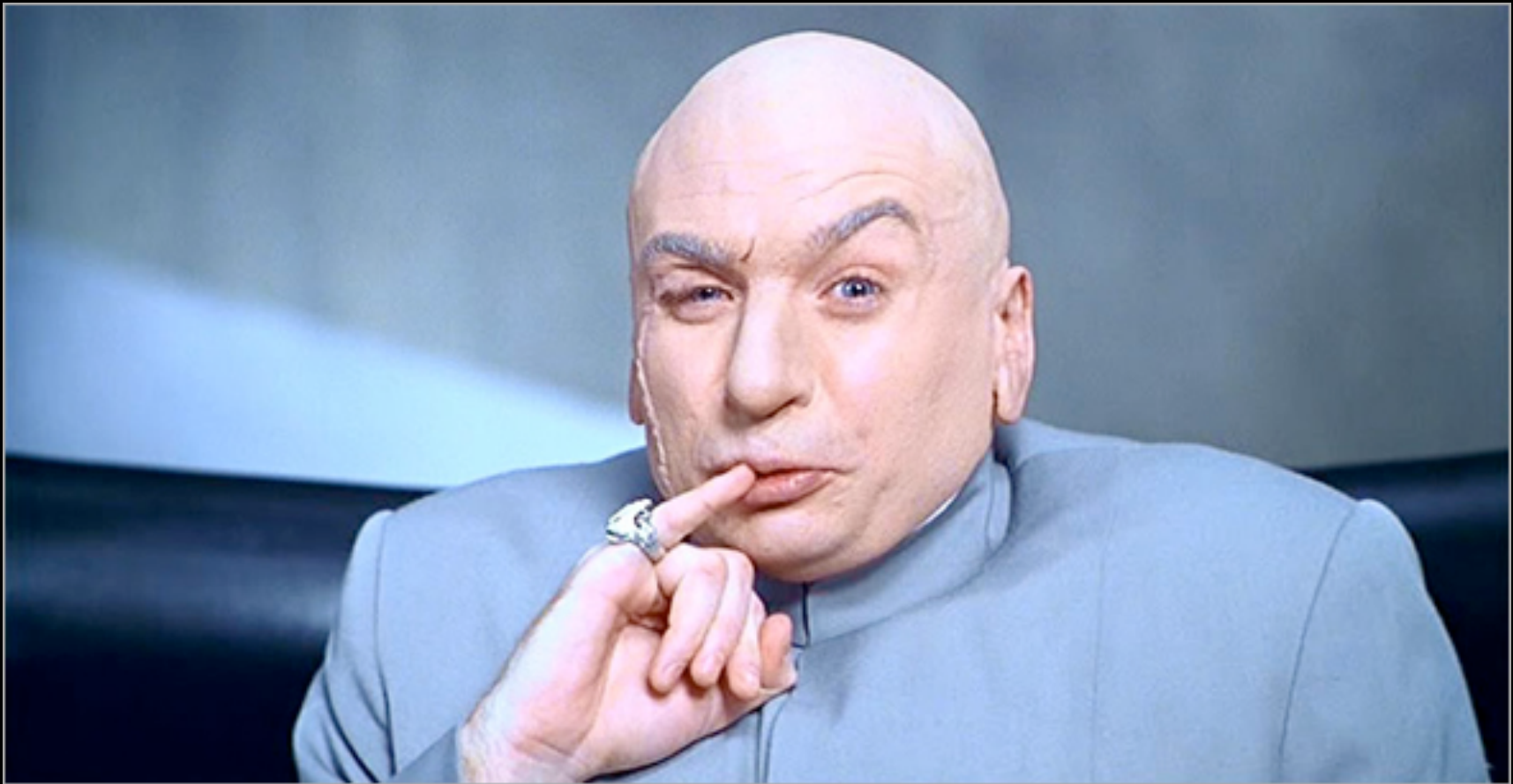
Addiction as a Brain Disease

***Utah Drug Court Conference
October 27, 2011***

***Kevin T. McCauley, M.D.
The Institute for Addiction Study
kevintmccauley@hotmail.com***



“W.W.Dr.E.D.” (What would Dr. Evil do?)



The most evil disease imaginable ...

- Wouldn't look like a "disease" at all (nearly invisible epidemiologically)
- Genetic, but with variable penetrance (genotype \neq phenotype)
- Repulsive symptoms easily confused with "willful badness"
- Self-deception as a clinical feature
- Poor prognosis if untreated, but some will get better (inexplicably)
- Chronic and relapsing (not acute, nor cured)
- Culturally & politically divisive (would tap into society's deepest prejudices, stigma, superstitions and attack its core values)
- Would cover its tracks (by blaming other diseases)
- Would only submit to "weird" solutions: peer support, patient accountability, personal evaluation, and spiritual growth (not just a medication or surgery)

Leading Causes of Death

1. Heart Disease
2. Cancer
3. Stroke/HTN

Leading Causes of Death

1. Heart Disease

2. Cancer

3. Stroke/HTN

OBESITY

NICOTINE/ALCOHOL

ALL OF THE ABOVE

Leading Causes of Death

1. Heart Disease

ADDICTION

2. Cancer

ADDICTION

3. Stroke/HTN

ADDICTION

Leading Causes of Death

1. Heart Disease	ADDICTION
2. Cancer	ADDICTION
3. Stroke/HTN	ADDICTION
4. Chronic Lung Disease	ADDICTION
5. Accidents	ADDICTION
11. Suicide	ADDICTION
12. Liver Disease/Cirrhosis	ADDICTION
14. Homicide	ADDICTION

EVERY DOCTOR IN PRIVATE PRACTICE WAS ASKED!



Family doctors, surgeons, diagnosticians, nose and throat specialists... doctors in every branch of medicine were asked: "What cigarette do you smoke, Doctor?"

Three nationally known independent research organizations did the asking.

The answers came in by the thousands. Actual statements from doctors themselves. Figures were checked and re-checked! The results? Camels... convincingly!

R. J. Reynolds Tobacco Co., Winston-Salem, North Carolina

According to this recent Nationwide survey:

MORE DOCTORS SMOKE CAMELS THAN ANY OTHER CIGARETTE!

This is no casual claim. It's an actual fact. Based on the statements of doctors themselves to three nationally known independent research organizations.

THE QUESTION was very simple. One that you...any smoker...might ask a doctor: "What cigarette do you smoke, Doctor?"

After all, doctors are human too. Like you, they smoke for pleasure. Their taste, like yours, enjoys the pleasing flavor of costlier tobaccos. Their throats too appreciate a cool mildness.

And more doctors named Camels than any other cigarette!

If you are a Camel smoker, this preference for Camels among physicians and surgeons will not surprise you. But if you are not now smoking Camels, by all means try them. Compare them critically in your "T-Zone" (see right).

CAMEL—COSTLIER TOBACCOS

THE "T-ZONE" TEST WILL TELL YOU

The "T-Zone"—T for taste and T for throat—is your own proving ground for any cigarette. Only your taste and throat can decide which cigarette tastes best to you... how it affects your throat. On the basis of the experience of many, many millions of smokers, we believe Camels will suit your "T-Zone" to a "T."

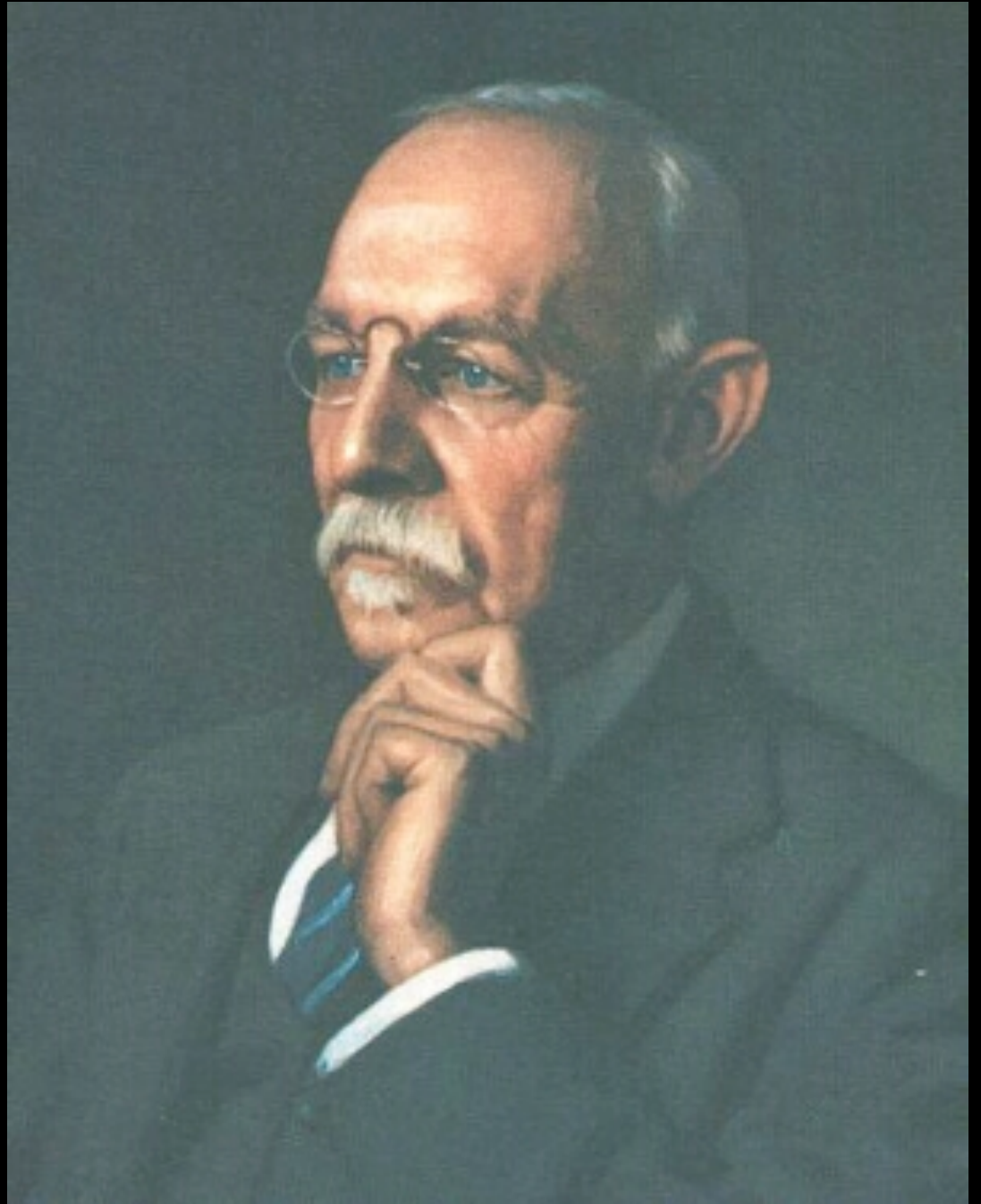


4011 25302189453-4

The Four Doctors, John Singer Sargent



***William S.
Halstead, M.D.
(The Father of
Modern Surgery)***



VMFAT-101 Sharpshooters MCAS El Toro, CA



United States Disciplinary Barracks Fort Leavenworth, Kansas



Is Addiction Really a “Disease?”









“Choice” vs. “Disease”









“Choice” vs. “Disease”

- **Free Will exists**
- **Responsibility**
- **Can stop**
- **Punishment and Coercion DO work**
- **BEHAVIORS**

- **No Free Will**
- **No Responsibility**
- **Can't stop**
- **Punishment and Coercion DON'T work**
- **SYMPTOMS**

The Prosecutors Challenges

1.

2.

3.

4.

5.

6.

The Prosecutors Challenges

1. The Outrage Argument

2.

3.

4.

5.

6.

The Prosecutors Challenges

1. The Outrage Argument

How dare you call addiction a “disease” – addicts are liars, cheats and thieves

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2. The Disease Nosology Argument

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Pedophiles have a disease – they suffer from pedophilia

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3. The “Punishment Works” Argument

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Most people quit when the consequences get bad enough

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4. The Accountability Argument

What’s to keep the addict from running to “disease” as an excuse for bad behavior?

5.

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The addict never should have taken that first drug/drink

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6. The Problem of Evil Argument

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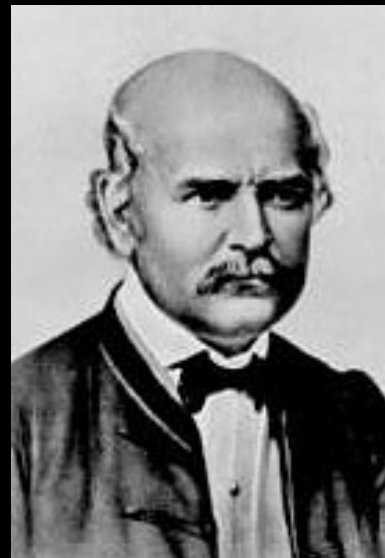
The addict never should have taken that first drug/drink

6. The Problem of Evil Argument

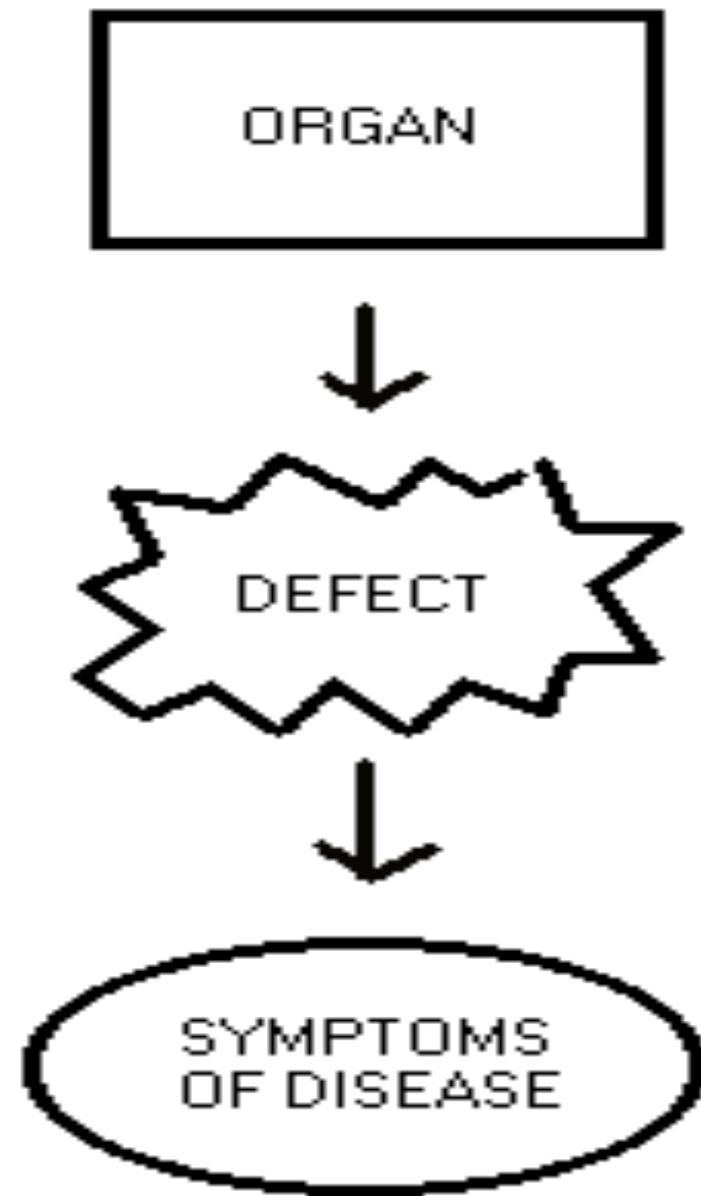
You’re just trying to explain away bad behavior

The Four Fathers of the “Disease Model”

Louie, Bobby, Rudy and Iggy



The “Disease Model”



Organ



Defect



Symptoms

Femur



Fracture



1. Screaming
2. Bleeding
3. Deformity
4. Disability

Pancreas

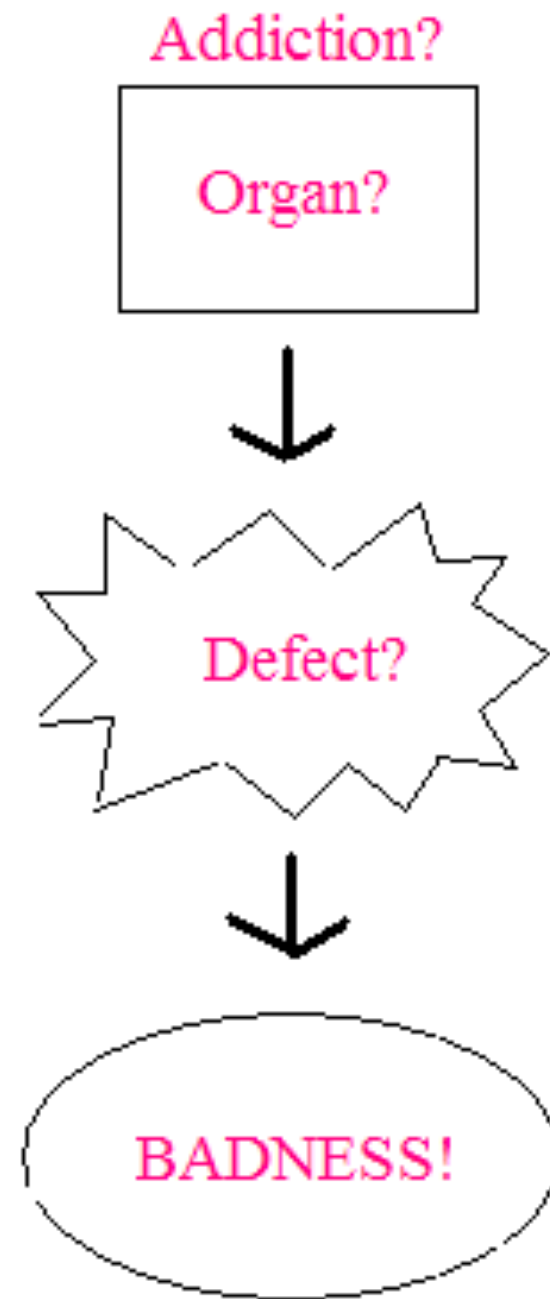
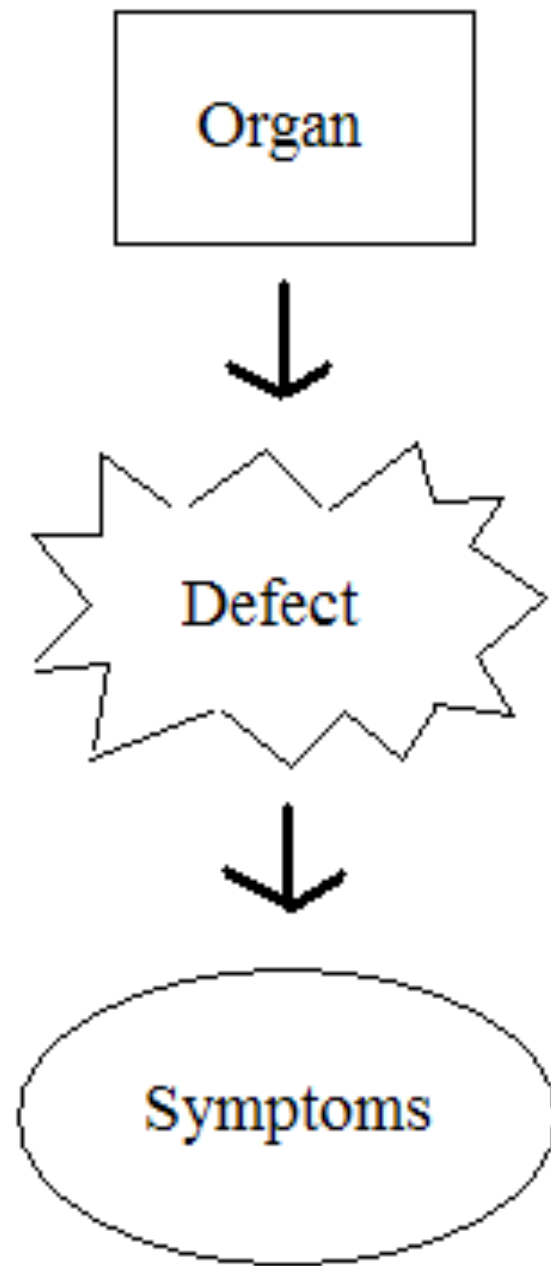


Islet Cell Death
No Insulin



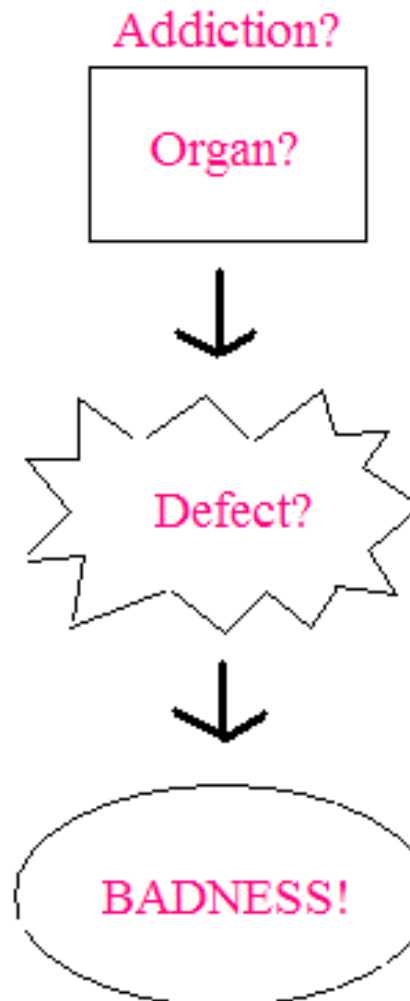
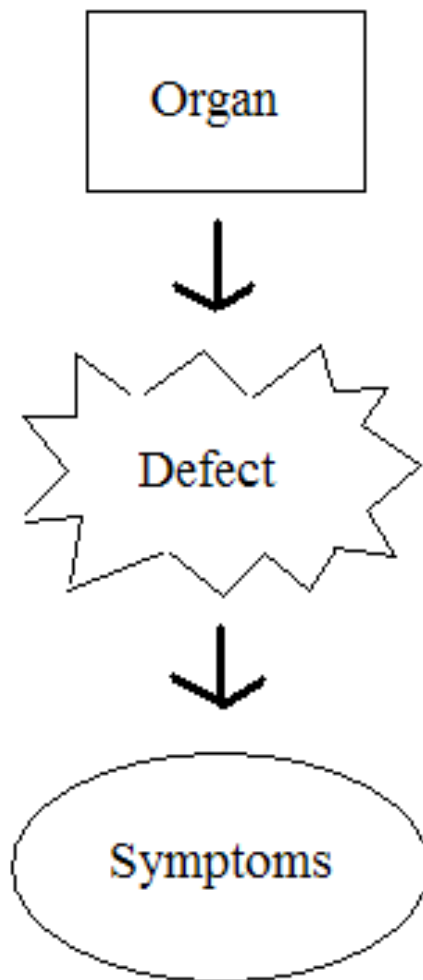
1. Elev. Blood Gluc.
2. Blurred Vision
3. Coma
4. etc.







If ever we could fit addiction into this model, then it would win admission into "The Disease Club" . . .



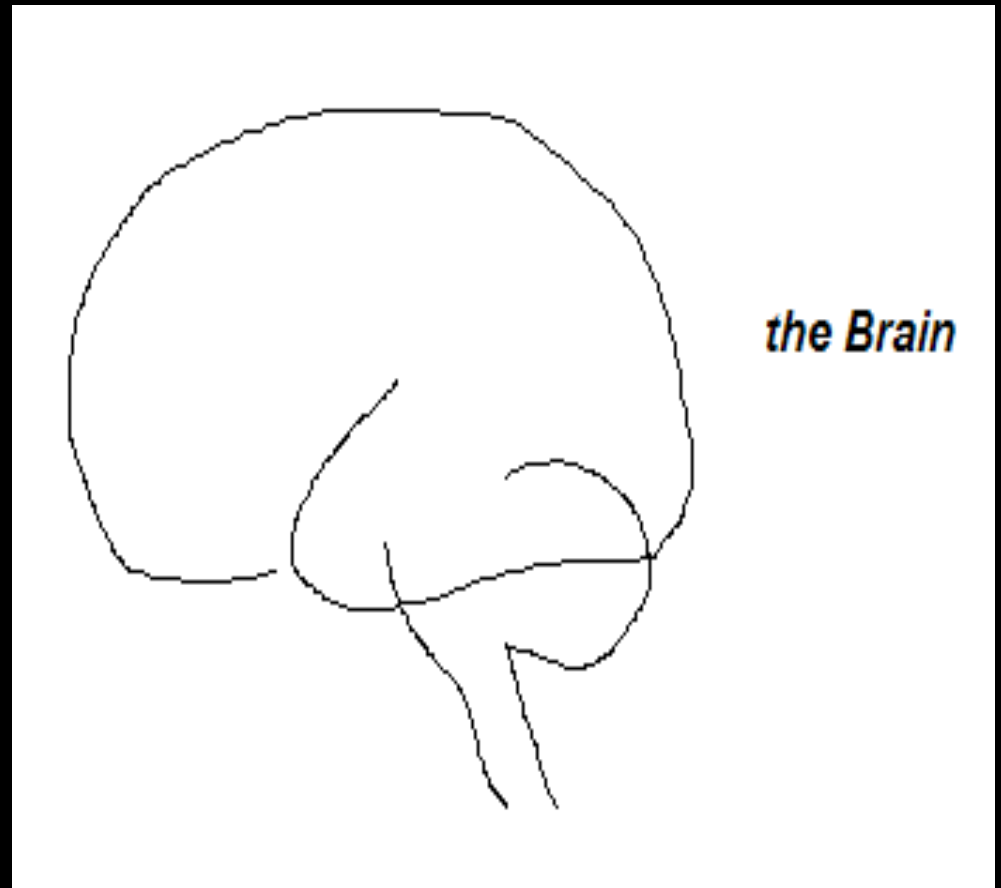
And now, we finally can ...

ASAM Addiction Definition (Aug 2011)

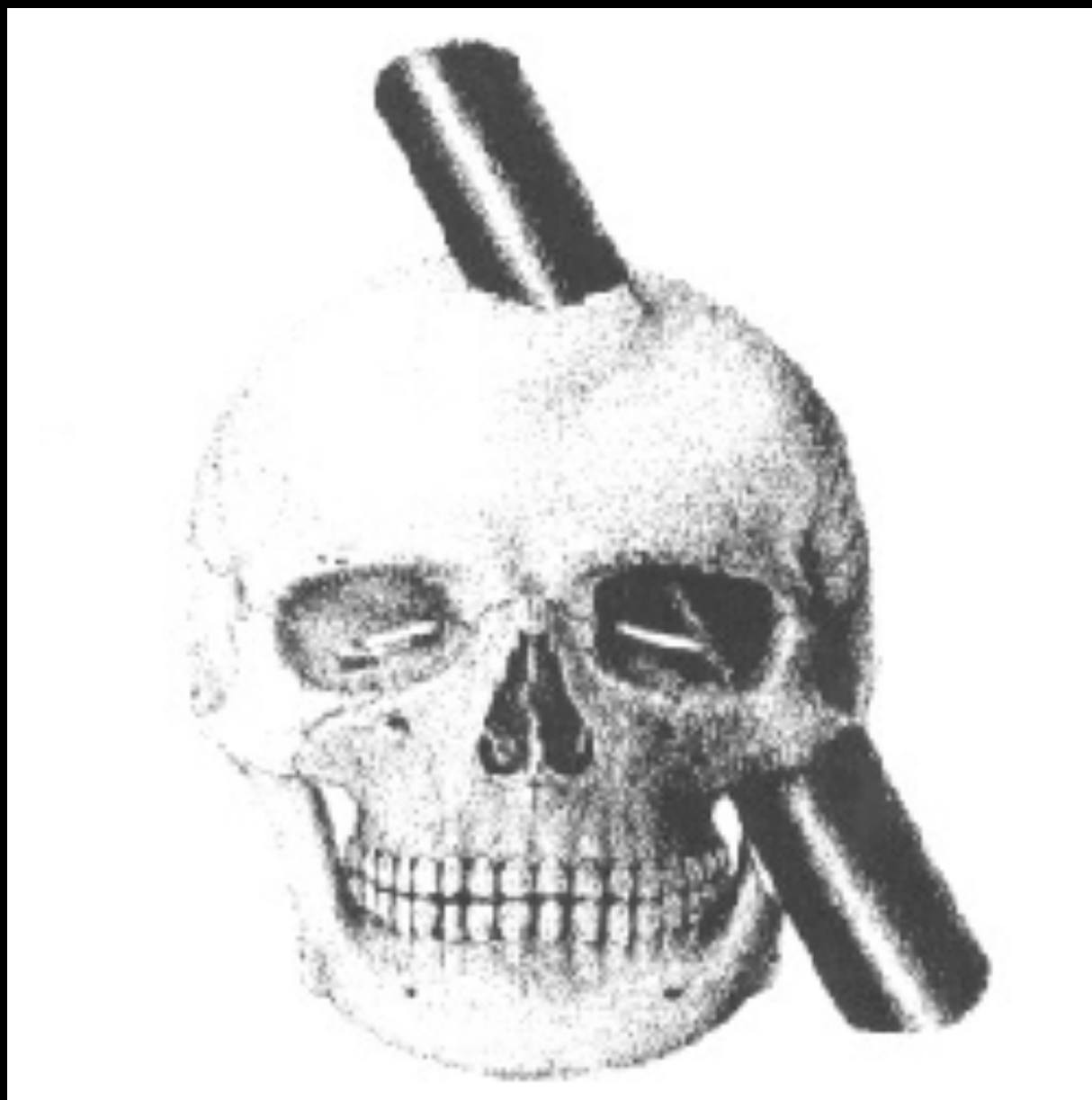
A primary, chronic and relapsing brain disease
of reward (nucleus accumbens),
memory (hippocampus & amygdala),
motivation and related circuitry (OFC, ACC, PFC)
that alters motivational hierarchies such that addictive
behaviors supplant healthy, self-care behaviors

Addiction is a BRAIN disease

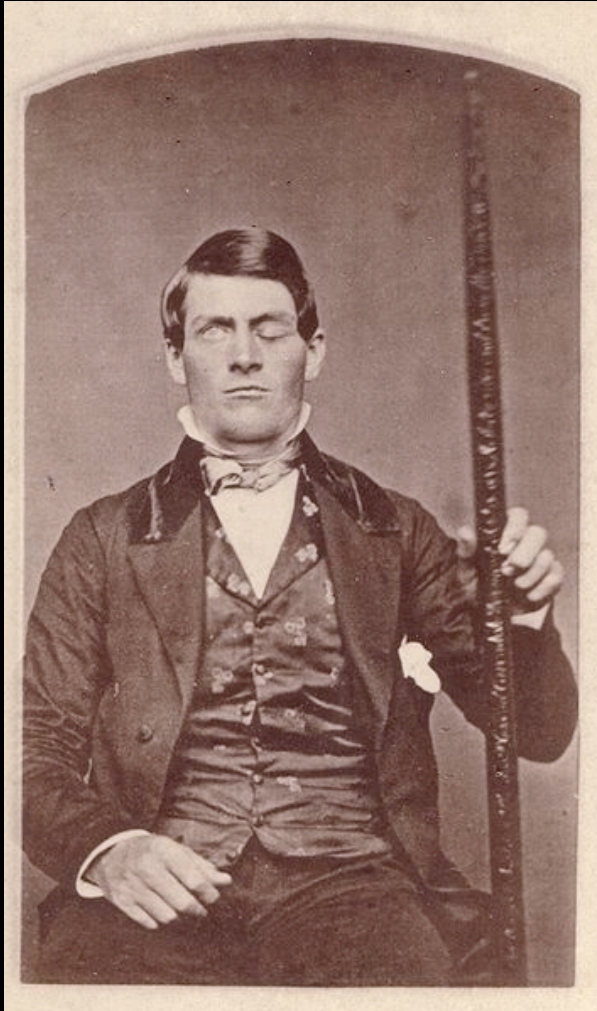
- ***The brain's a HARD organ***
- ***No good TESTS for brain diseases***
- ***People with brain diseases start out at a disadvantage***





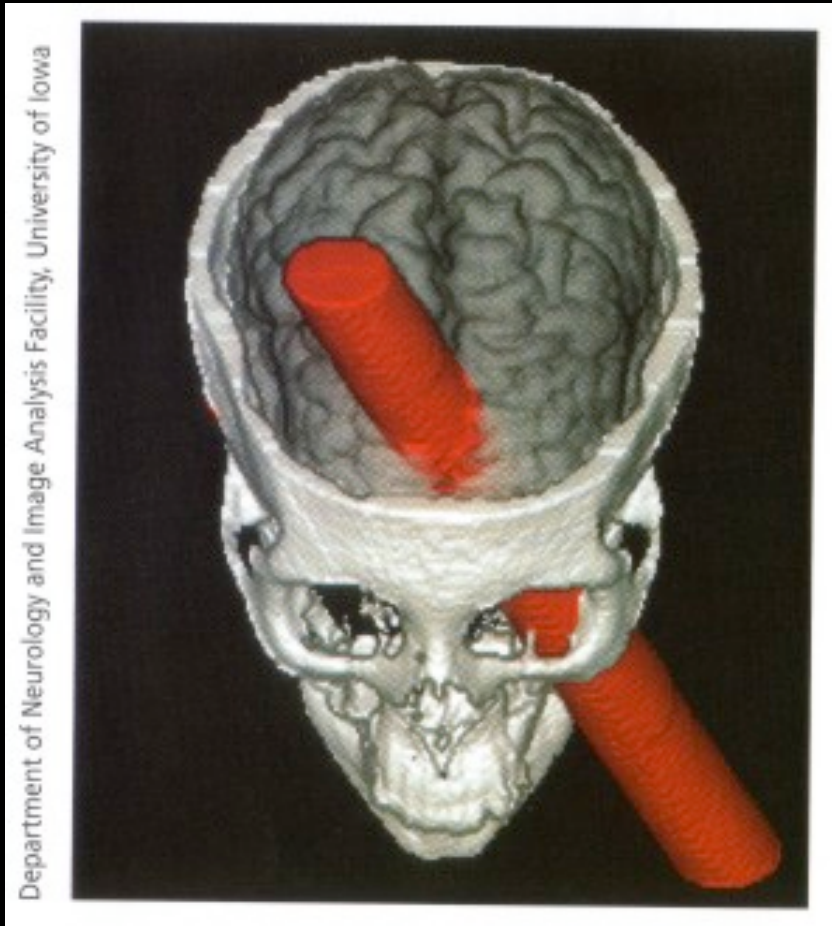


Phineas Gage (1823 – 1860)

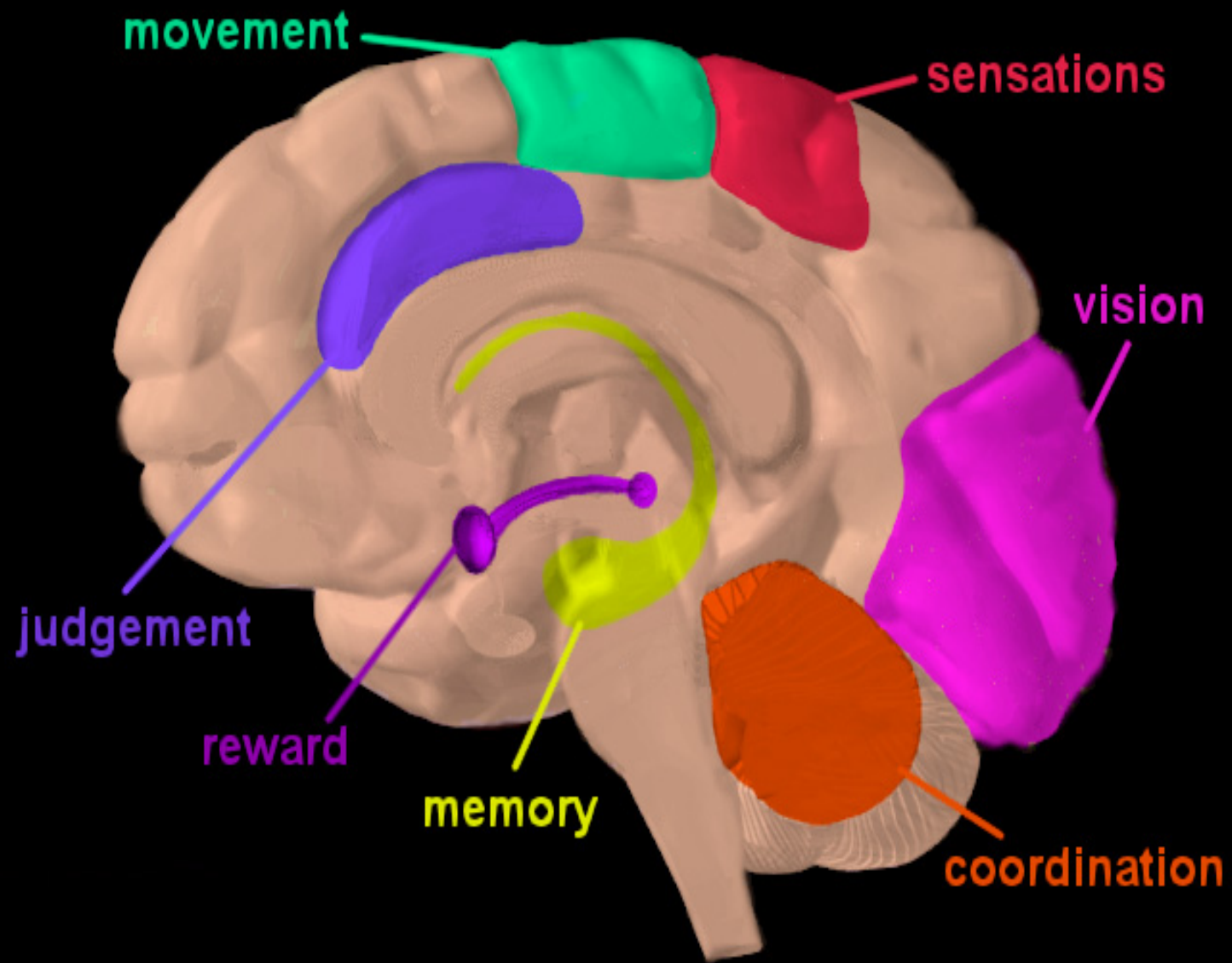


- Railroad construction foreman in Vermont
- Tamping rod driven through his skull by explosion
- Damage to Left Frontal Lobe and profound personality change
- “Gage was no longer Gage”

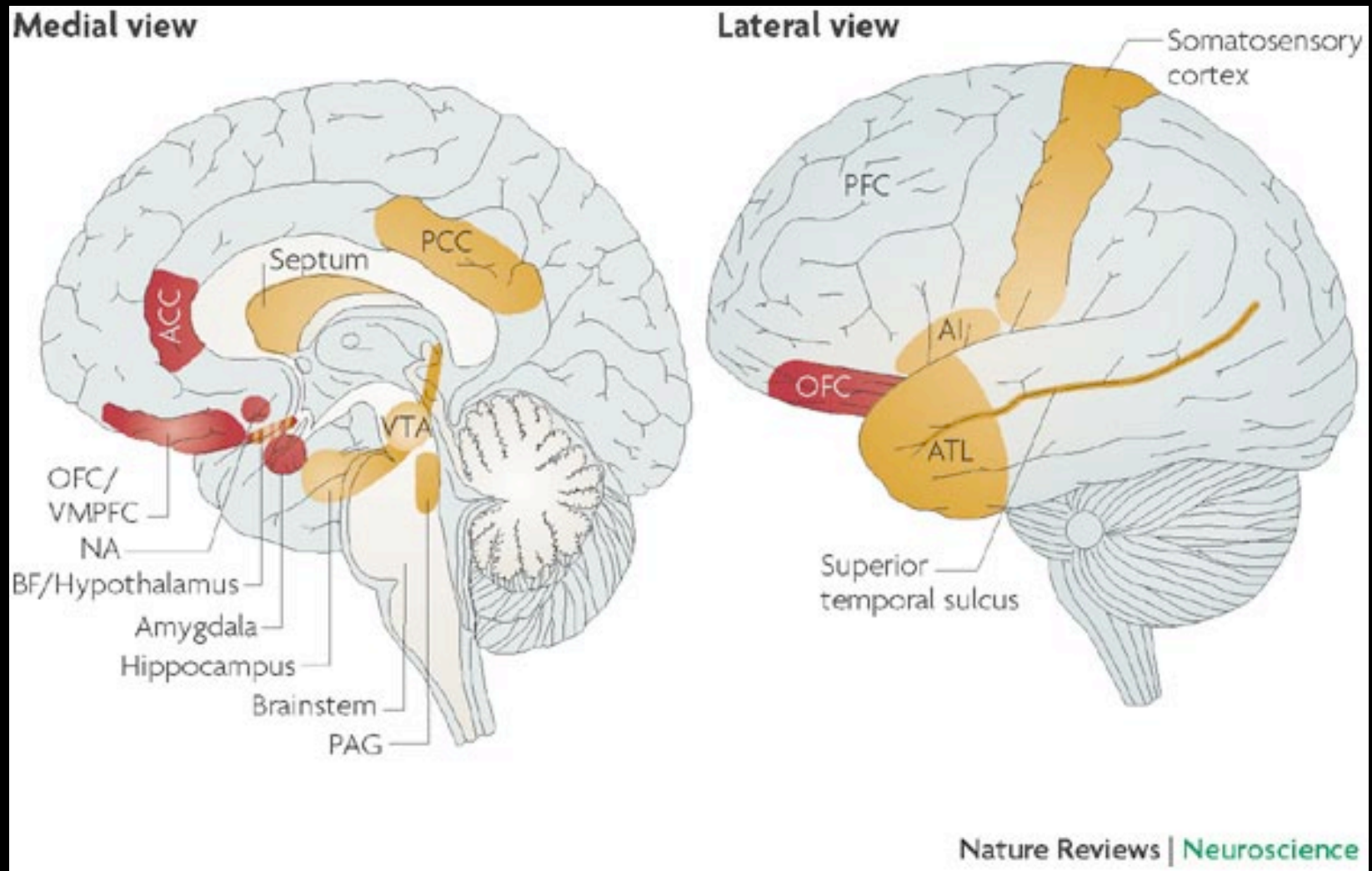
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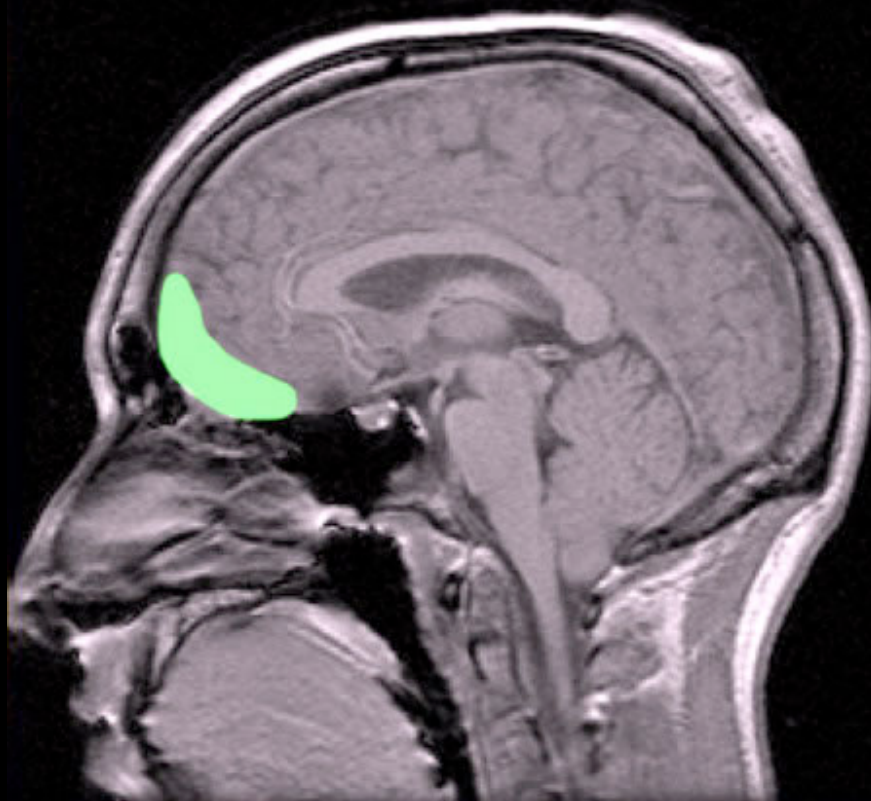
- **Damage to OFC**
- **Socially inappropriate**
- **Could not assign appropriate monetary value to objects**



The Key Parts of the Limbic Brain

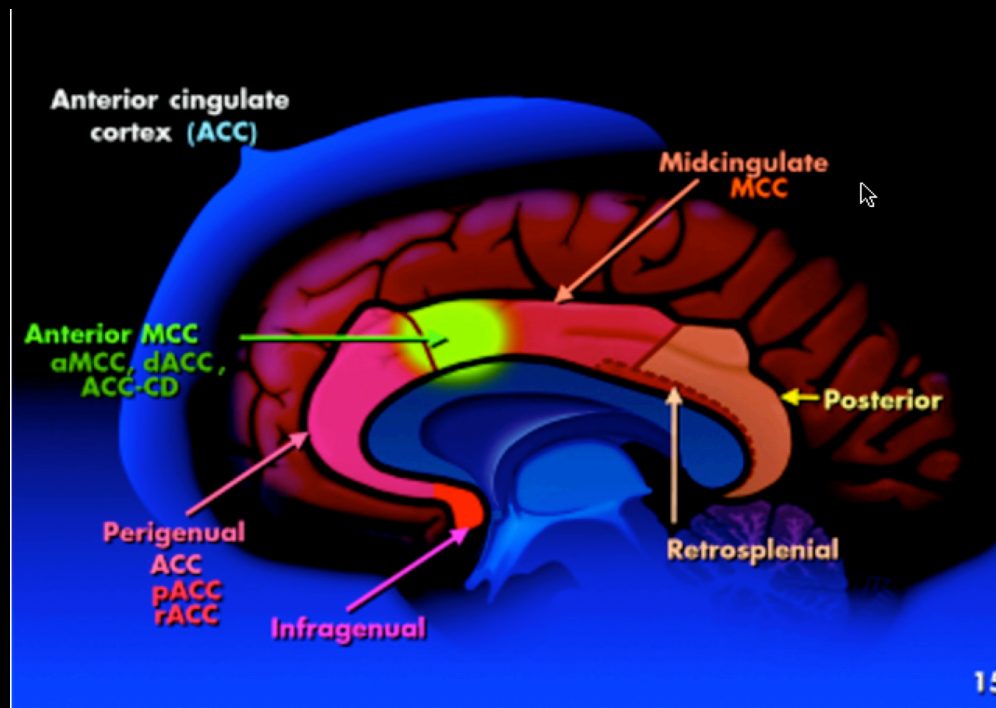


Orbitofrontal Cortex (OFC)



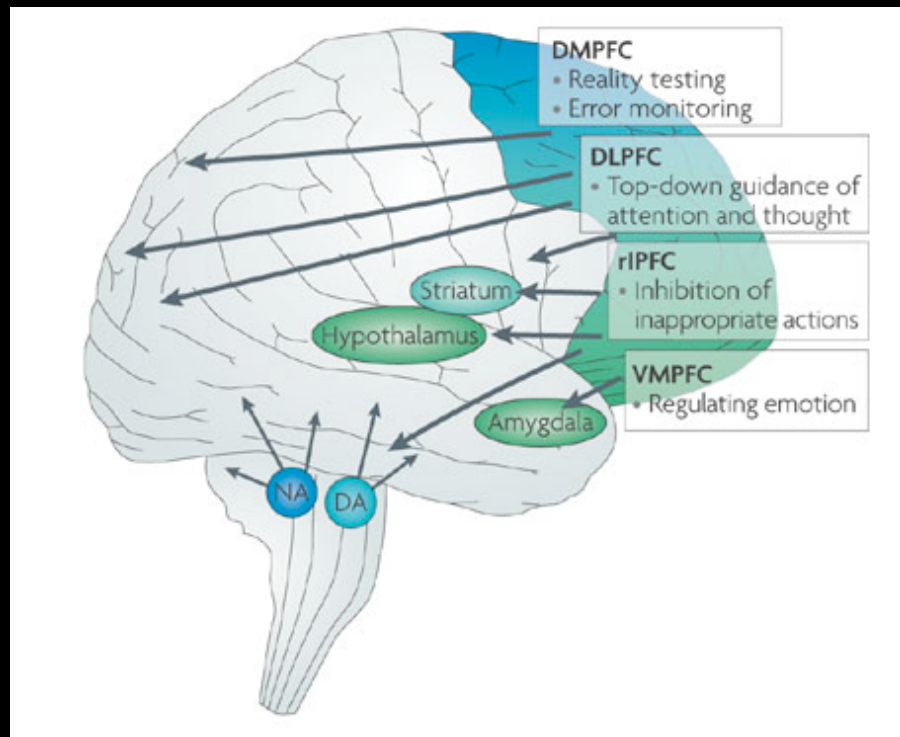
- Decision-making guided by rewards
- Integrates sensory and emotional information from lower limbic structures
- Flexible assignment of value to environmental stimuli to motivate or inhibit choices & actions
- Self-monitoring and social responding

Anterior Cingulate Cortex (ACC)



- Works with OFC: decision-making based on reward values
- But also generates new actions based on past rewards/punishments
- Appreciation and valuation of social cues
- MRI: active in tasks requiring empathy and trust

Prefrontal Cortex (PFC)



- Behavioral regulation
- Reflective decision-making
- Inhibition of socially inappropriate actions
- Emotional and sensory integration
- Planning complex behaviors
- Personality expression















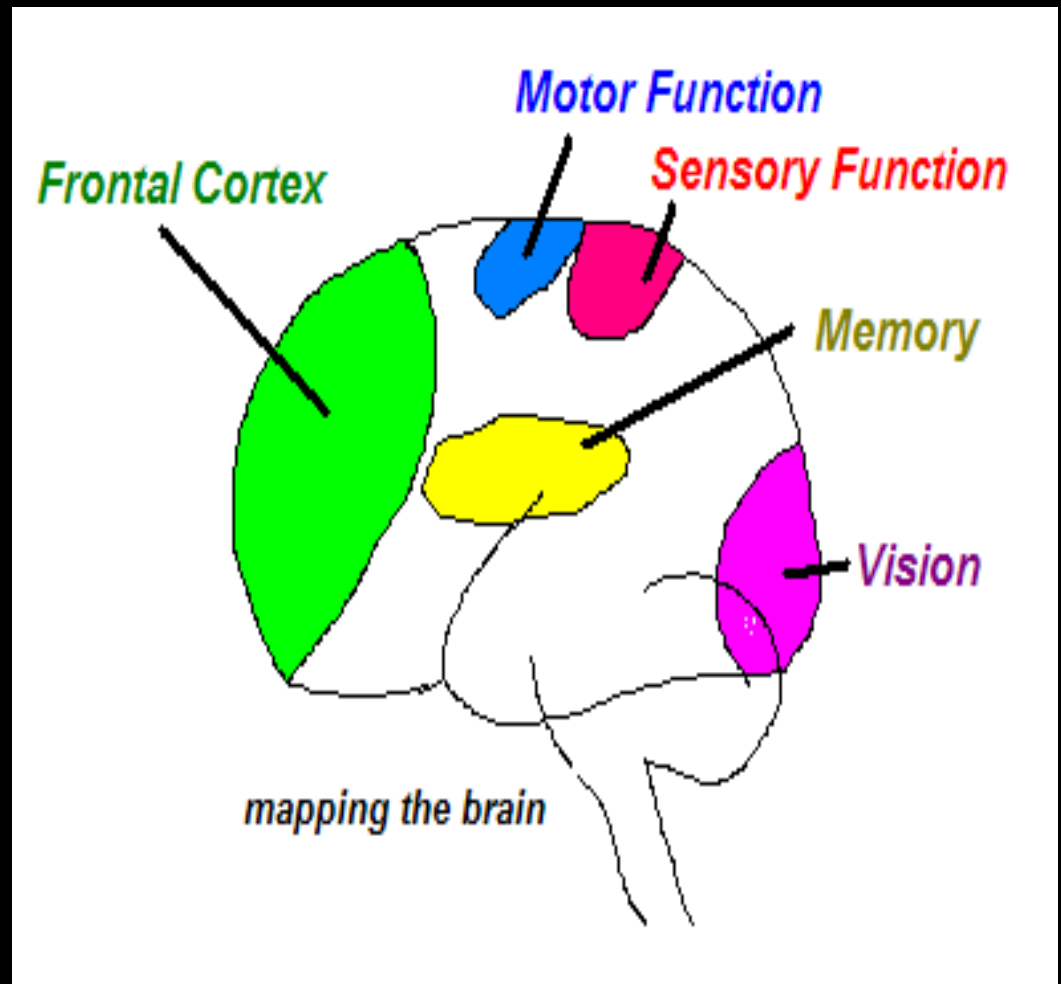






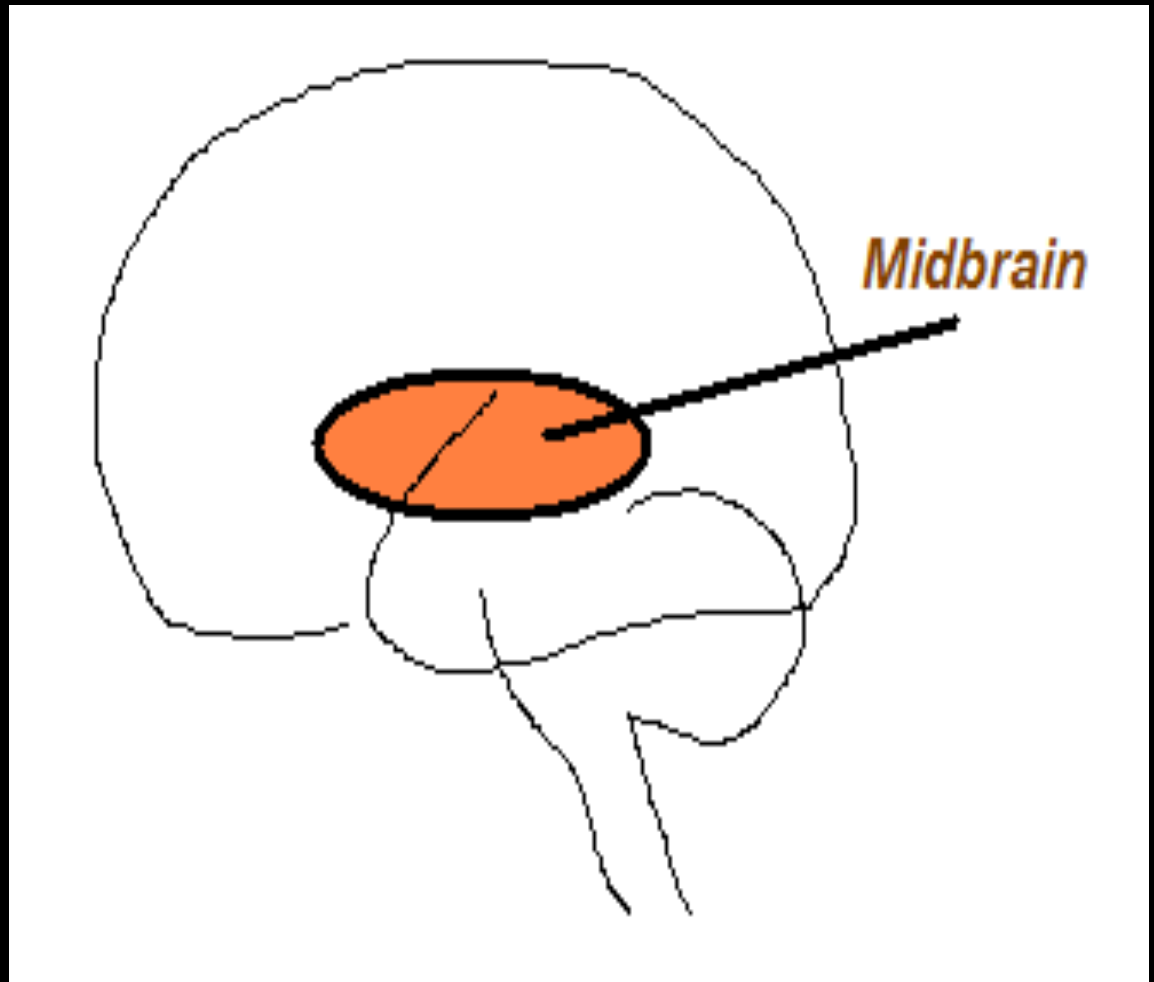
The Frontal Cortex: ***Defective in addiction?***

- ***Where drugs work?***
- ***Addict personality?***
- ***Sociopathy?***
- ***Self-centeredness?***
- ***Character defects?***
- ***Immorality?***
- ***Weak will?***
- ***Poor socialization?***
- ***Bad parenting?***



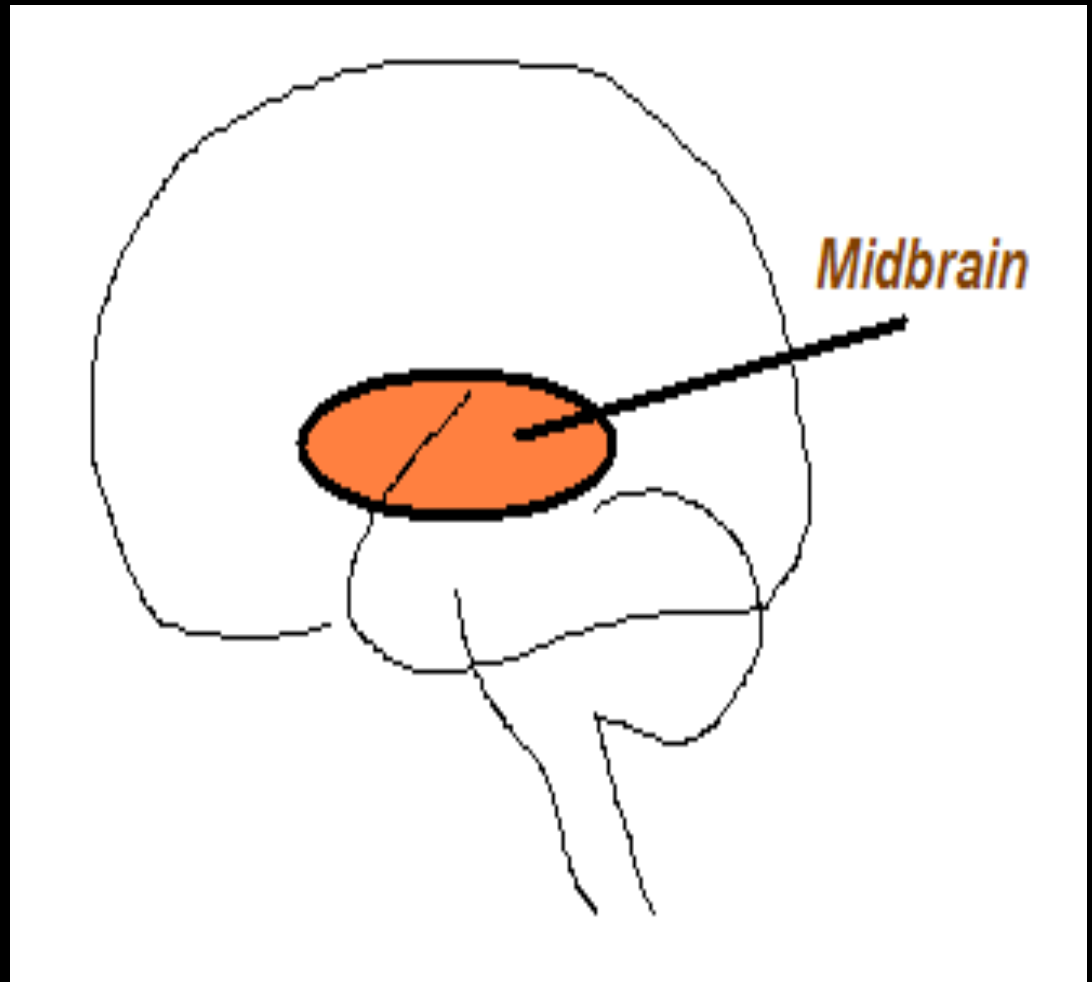
***But drugs don't work in the
Frontal Cortex . . .***

- ***Drugs work first in
the Midbrain***



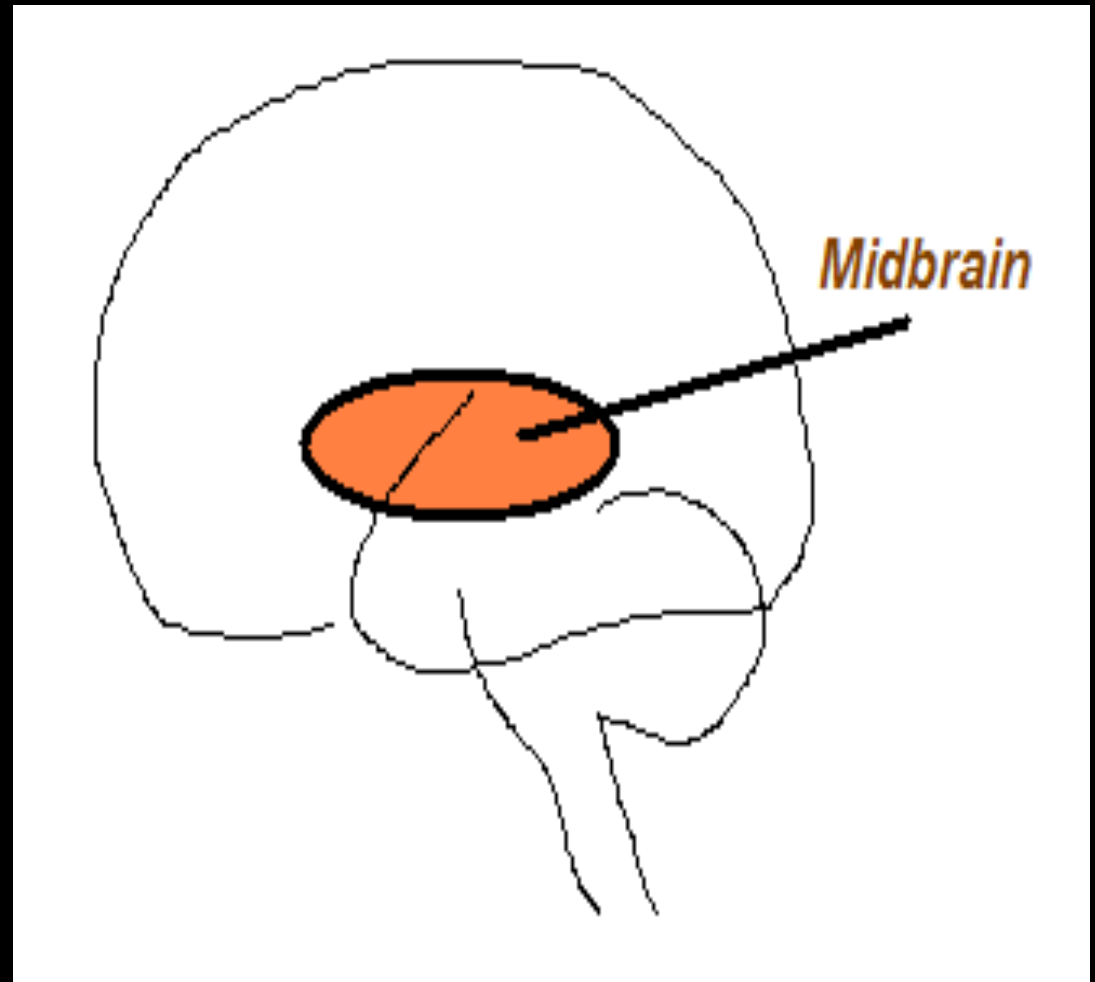
*The Midbrain is your **SURVIVAL** brain*
It handles:

- **EAT!**



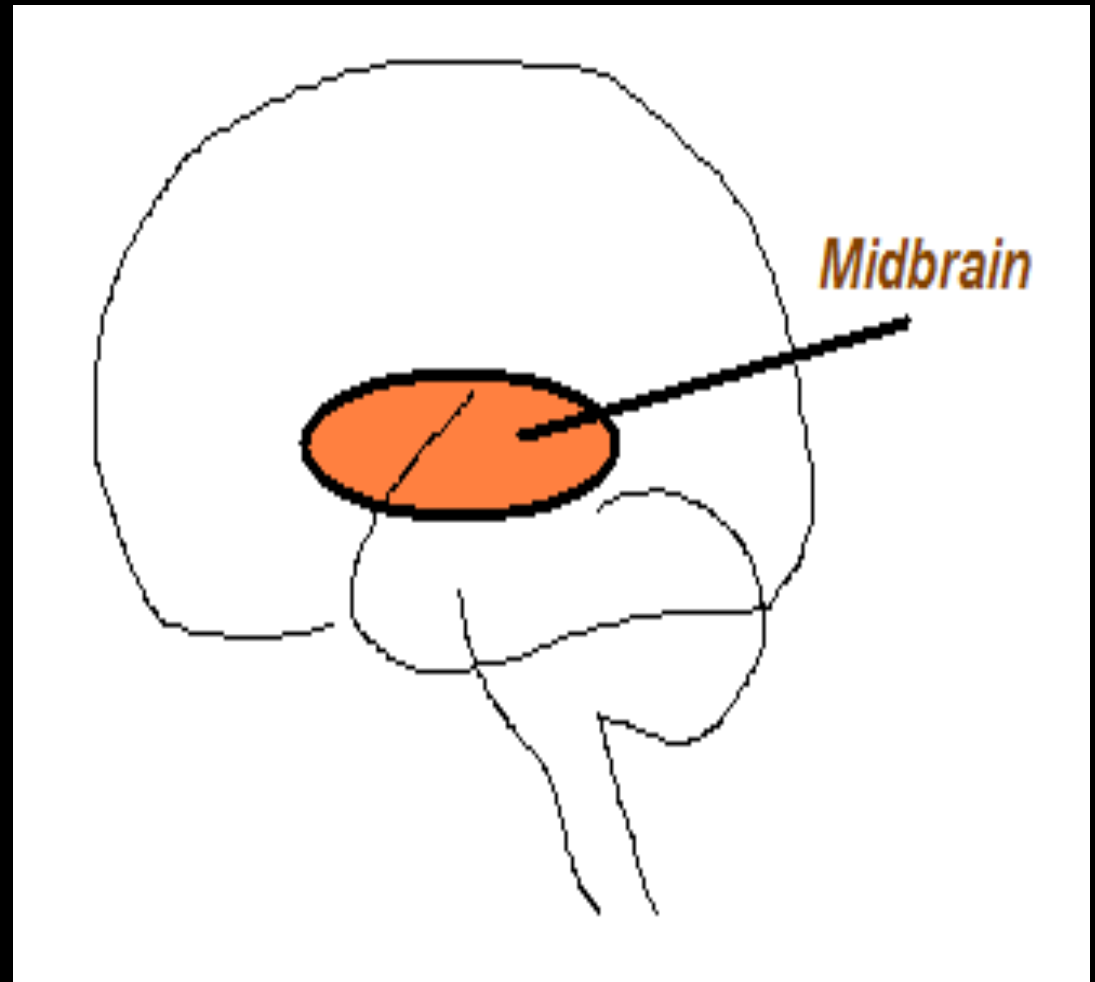
*The Midbrain is your **SURVIVAL** brain*
It handles:

- ***EAT!***
- ***KILL!***



*The Midbrain is your **SURVIVAL** brain*
It handles:

- **EAT!**
- **KILL!**
- **SEX !**









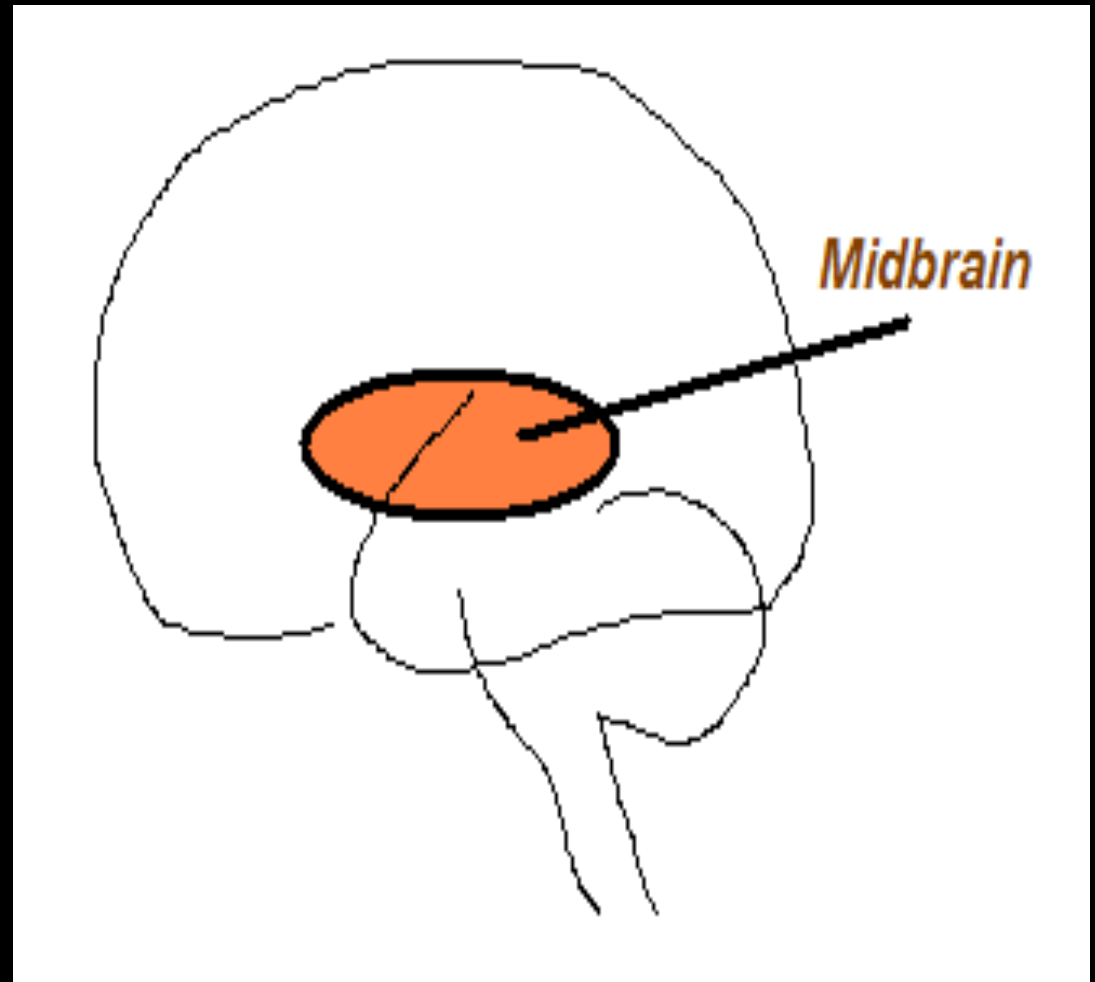






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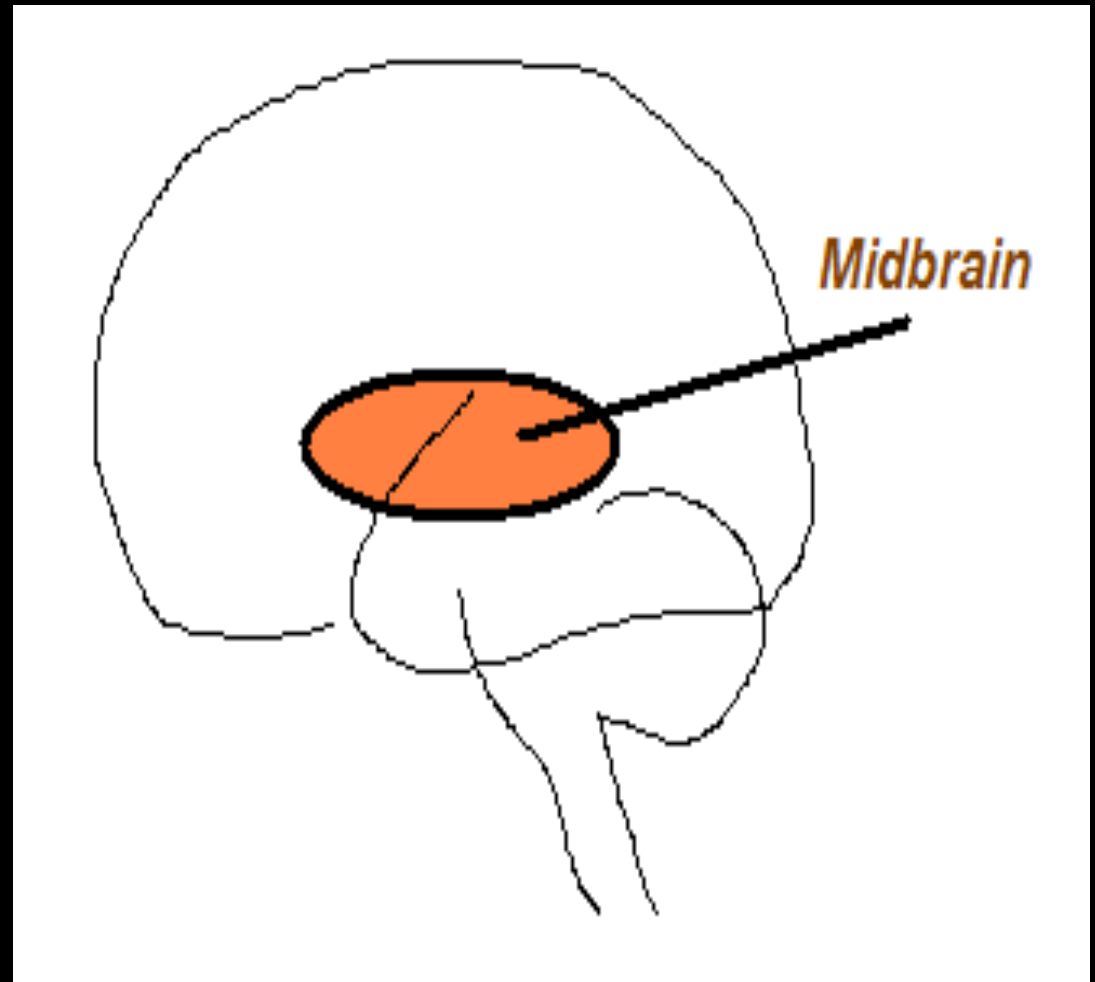






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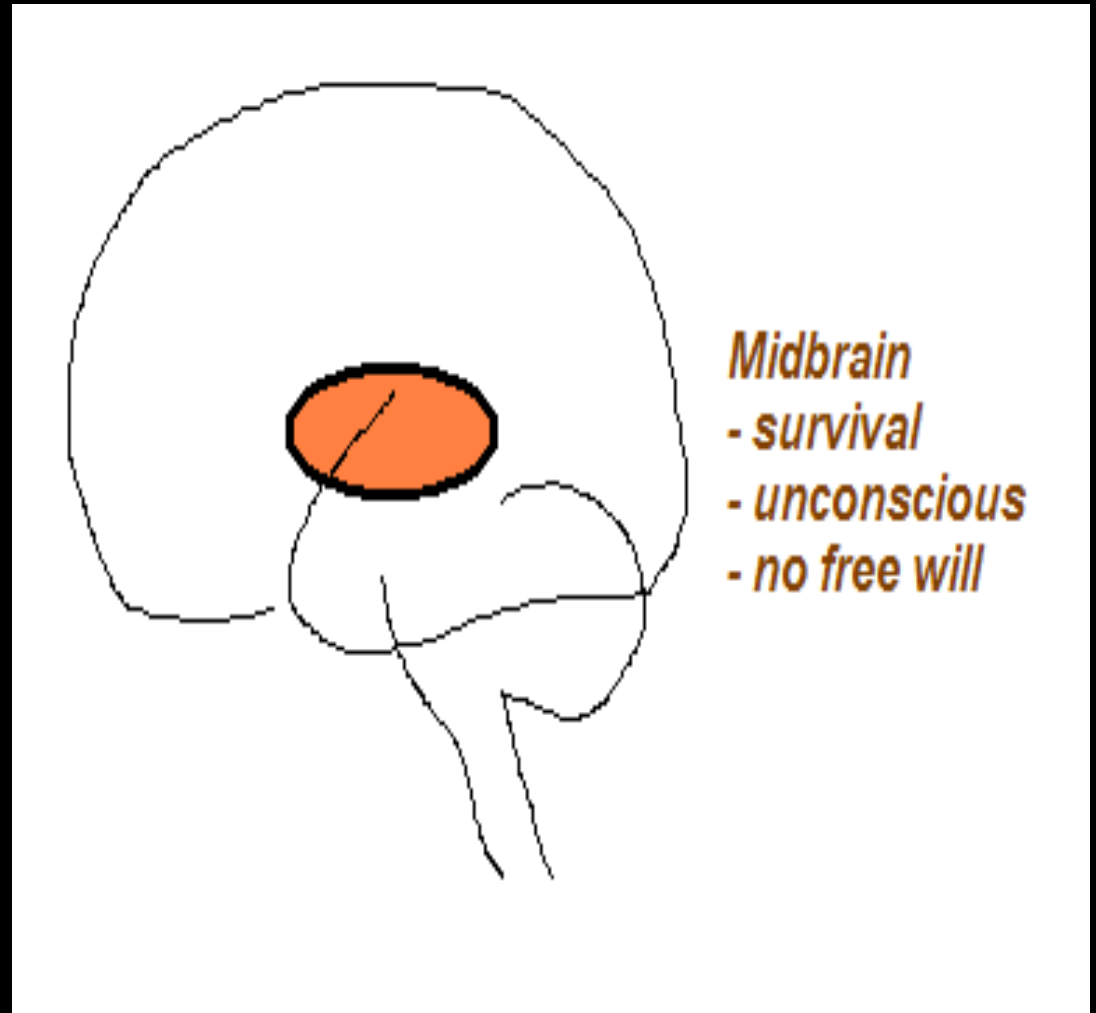
- **EAT!**
- **KILL!**
- **SEX !**

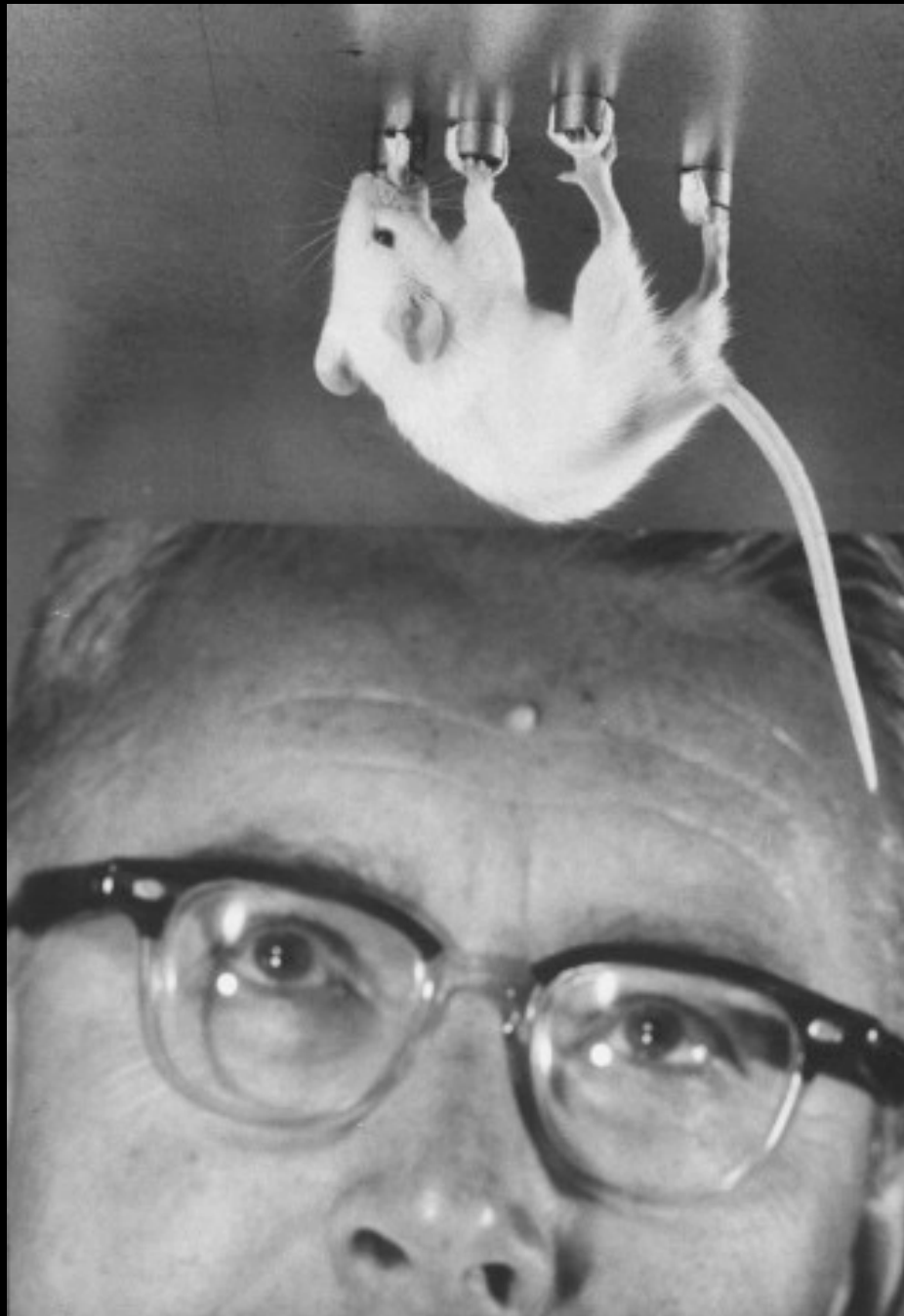


Drugs work in the Midbrain ...

- *... long before they work in the Cortex*

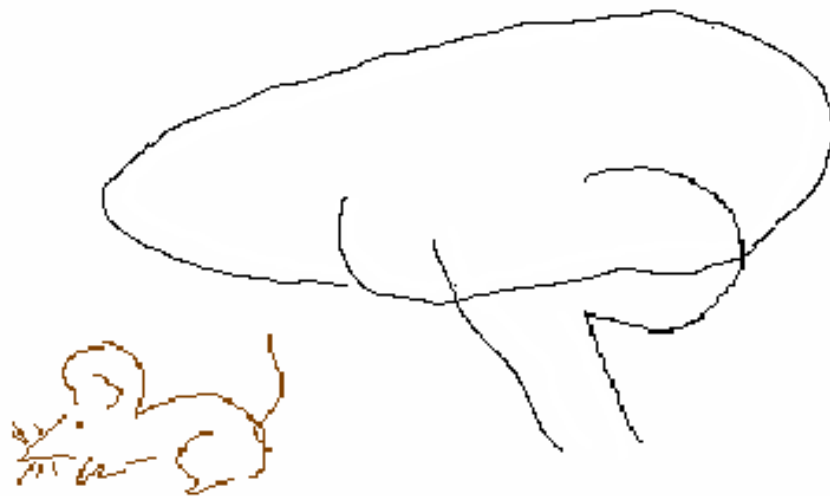
(and how do we know this? ...)



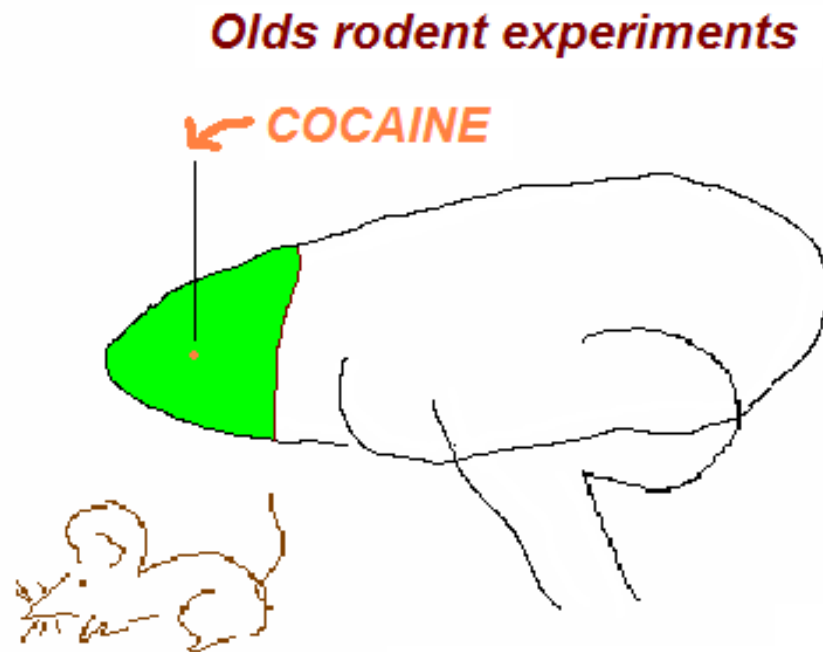


Where do mice self-administer drugs?

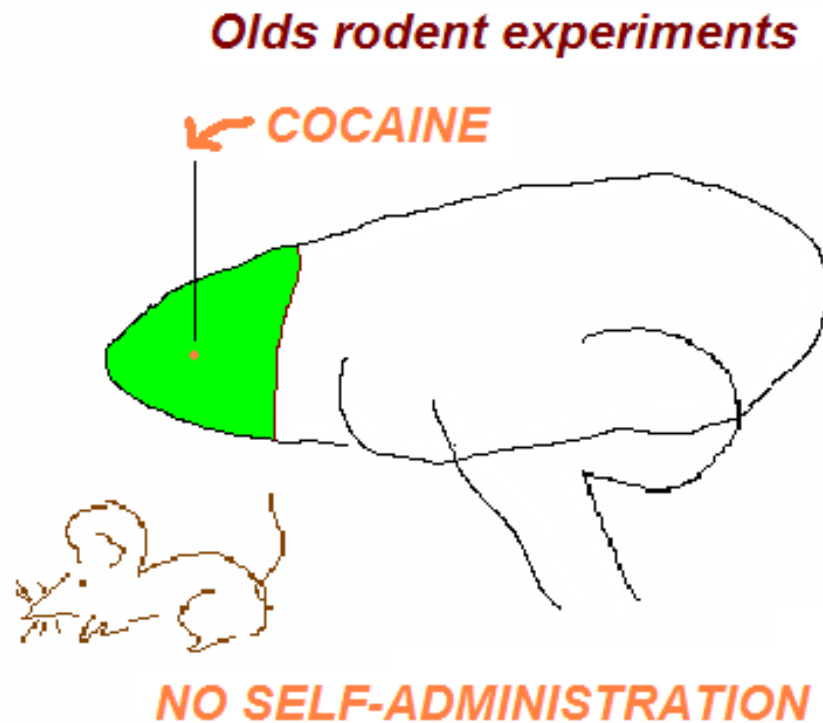
Olds rodent experiments



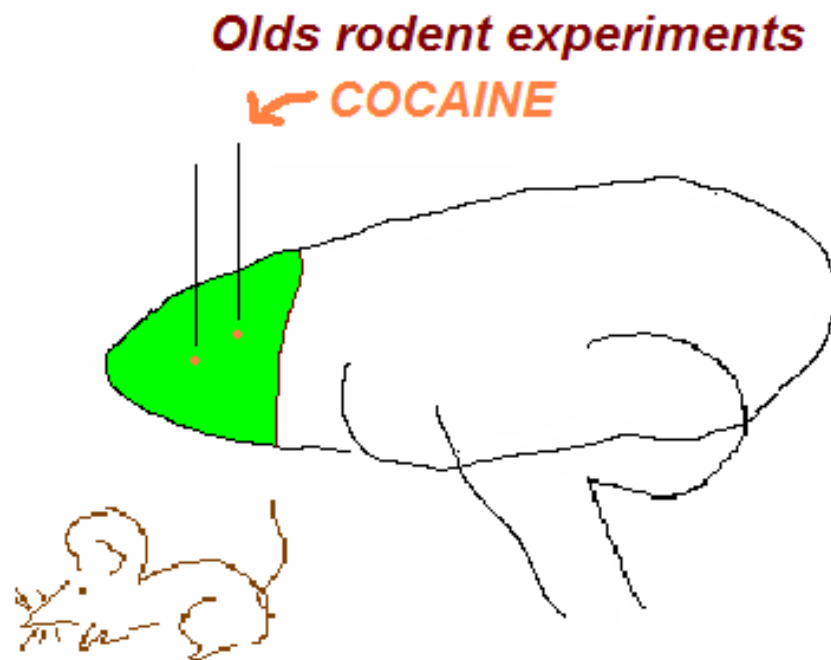
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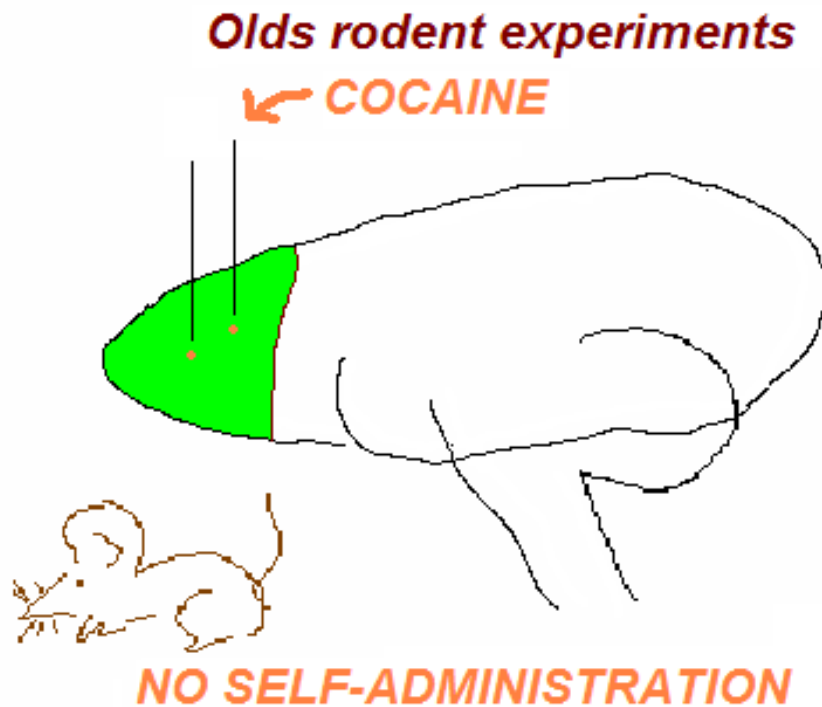
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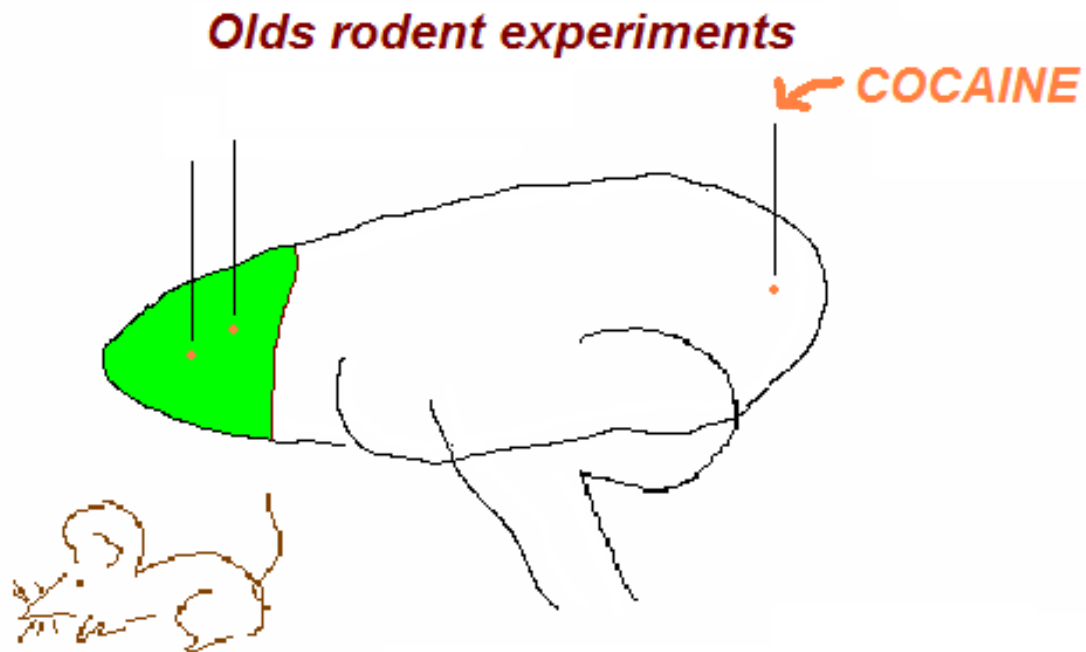
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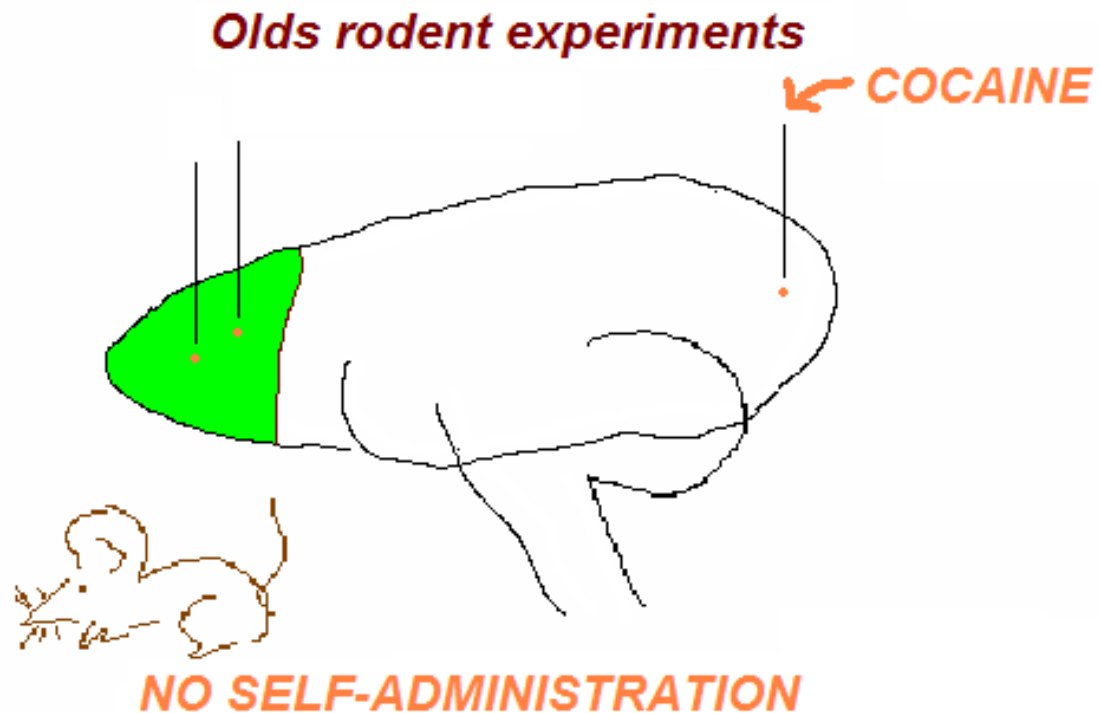
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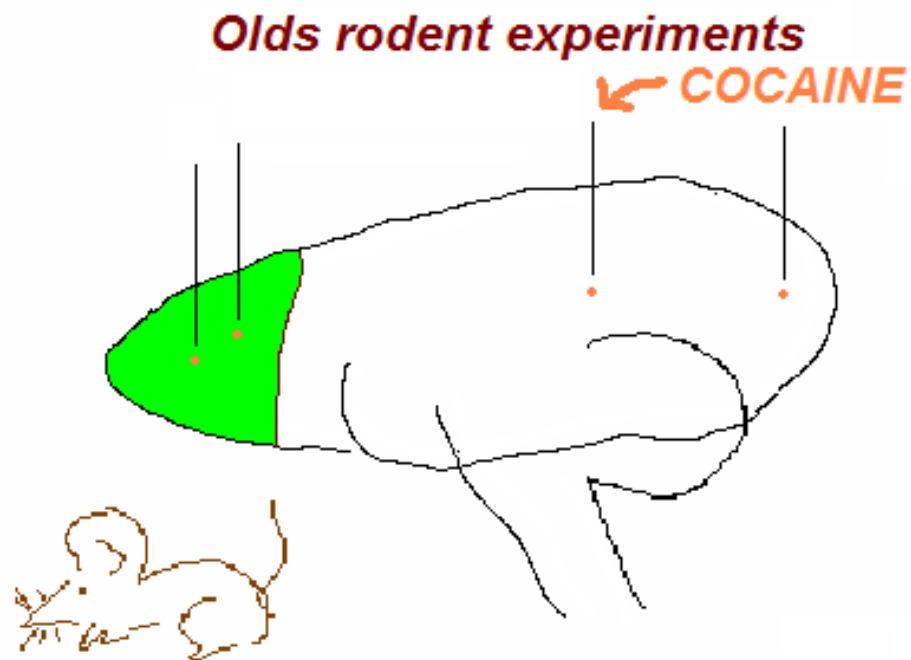
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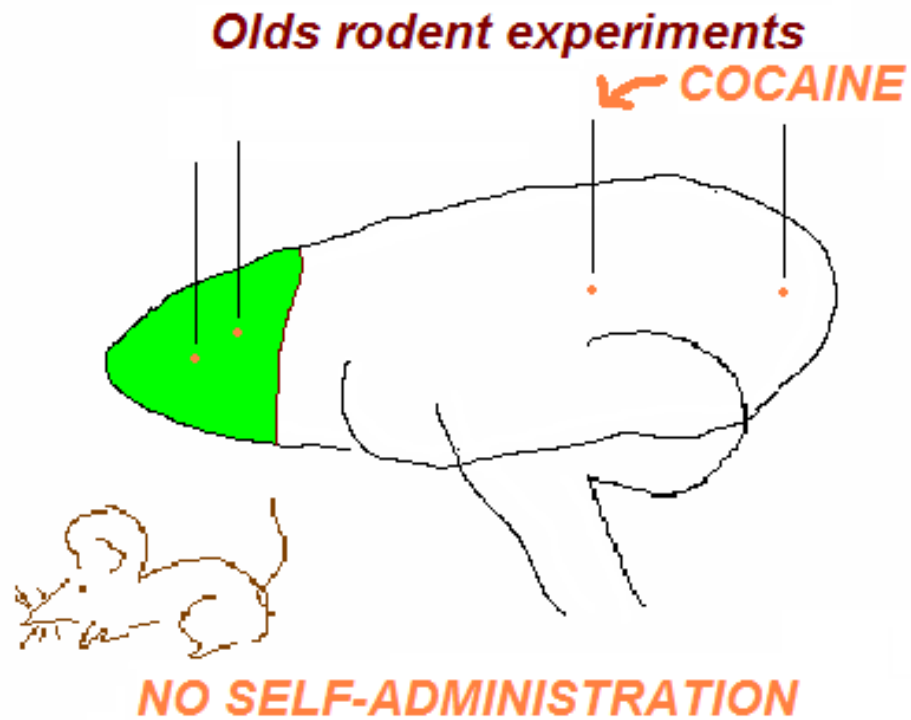
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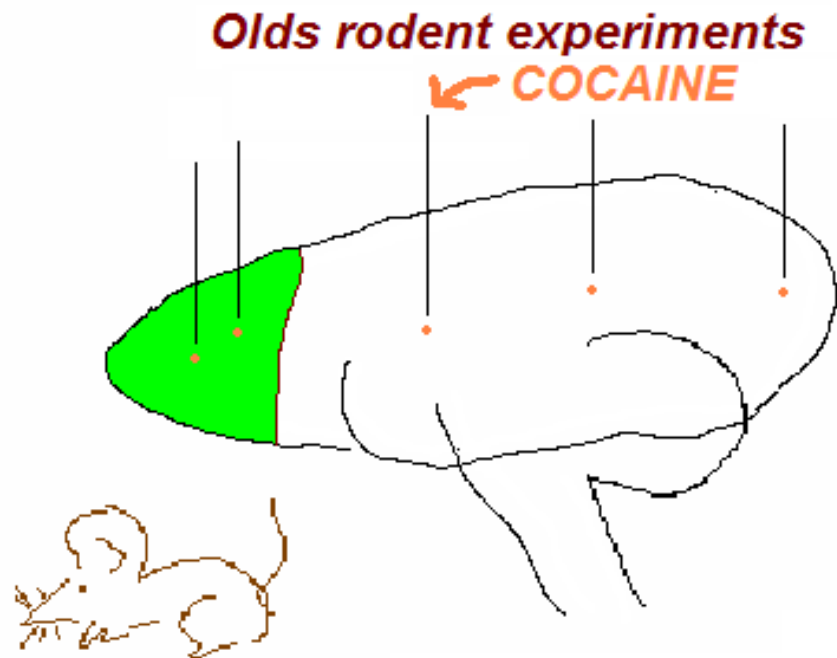
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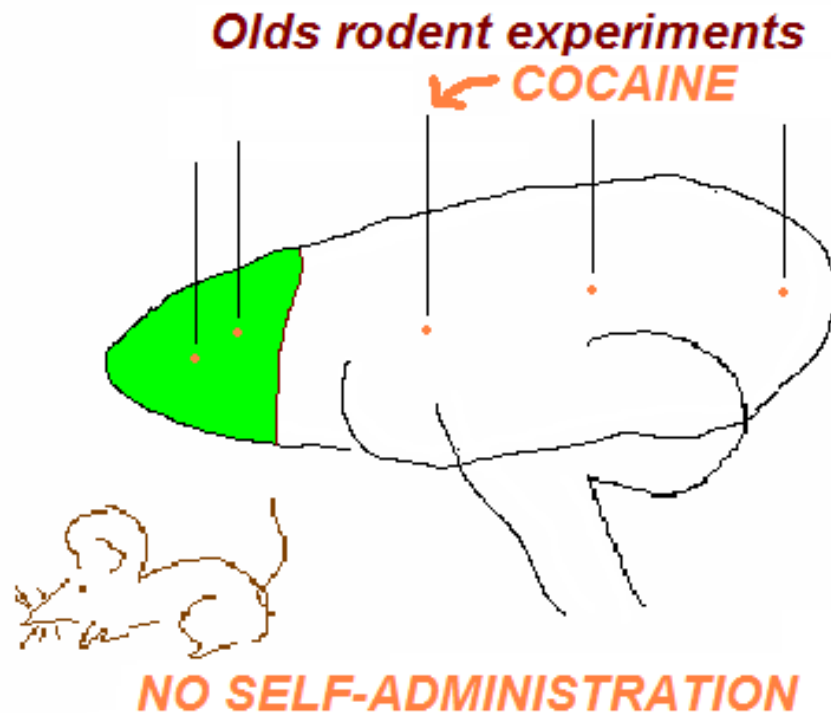
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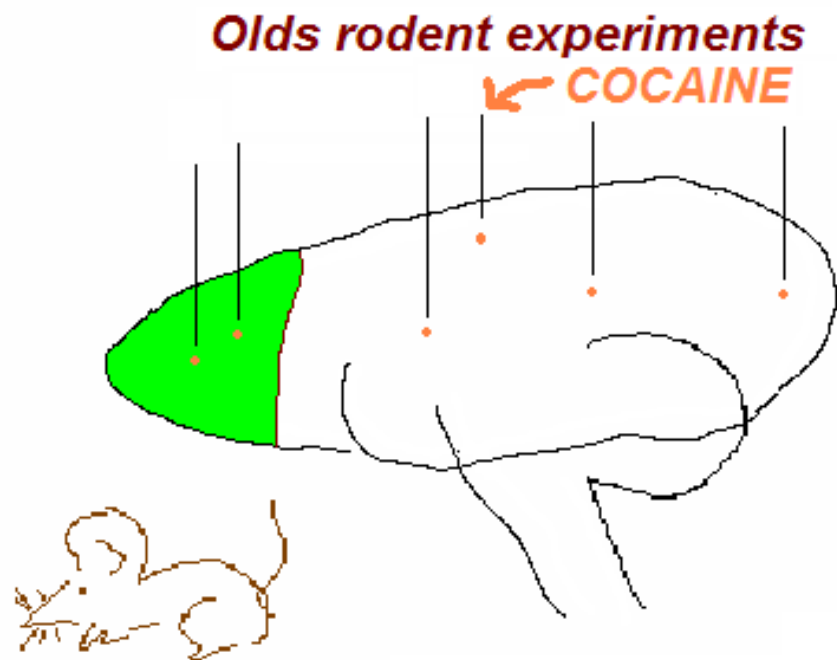
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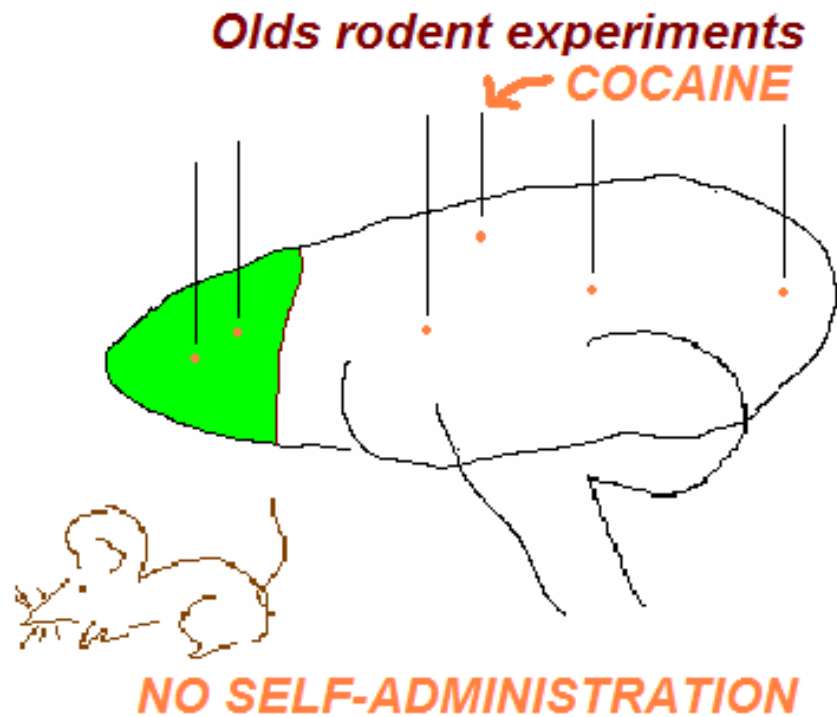
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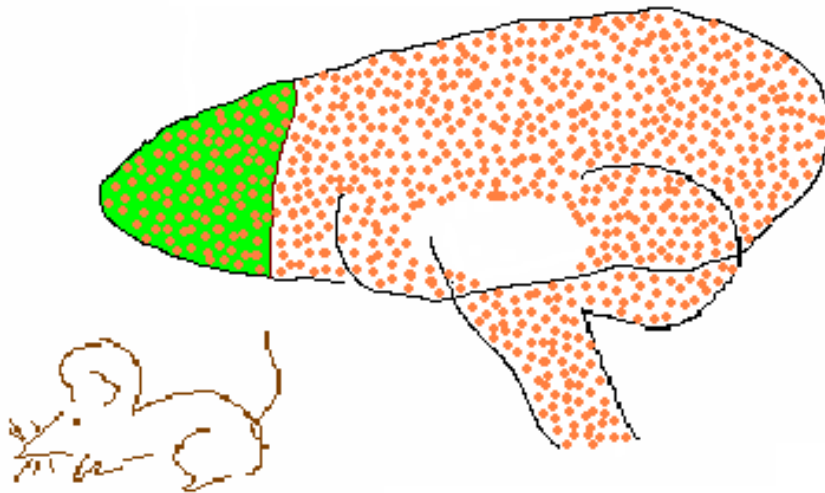


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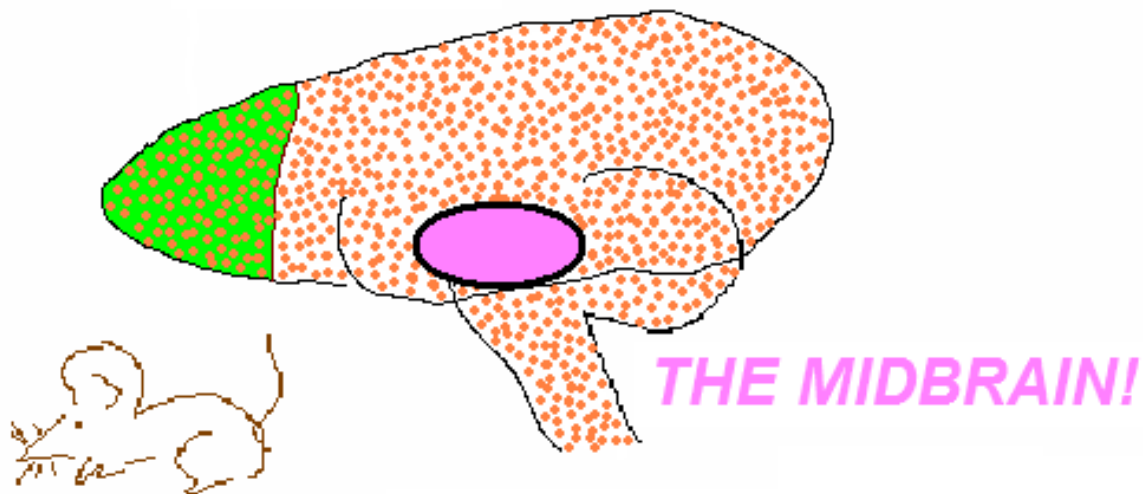
Olds experiments:

Olds rodent experiments

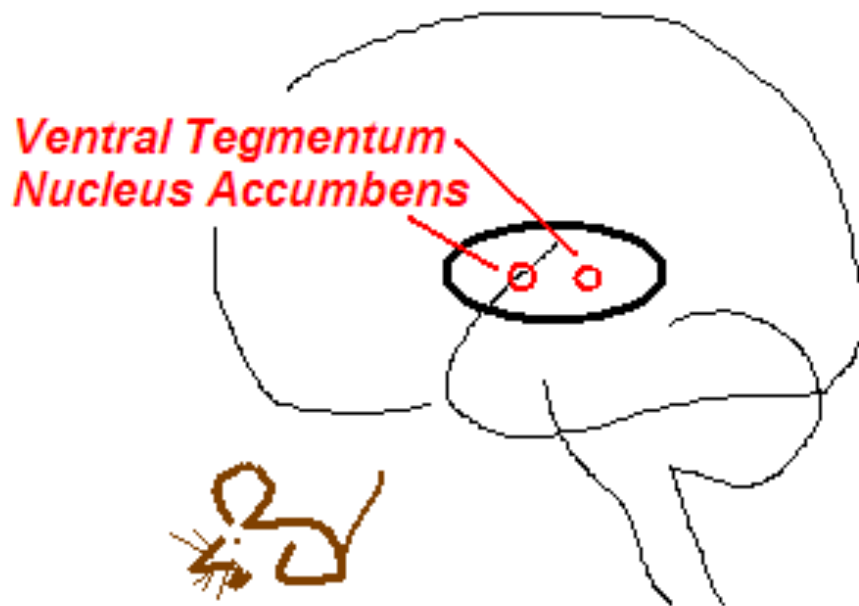


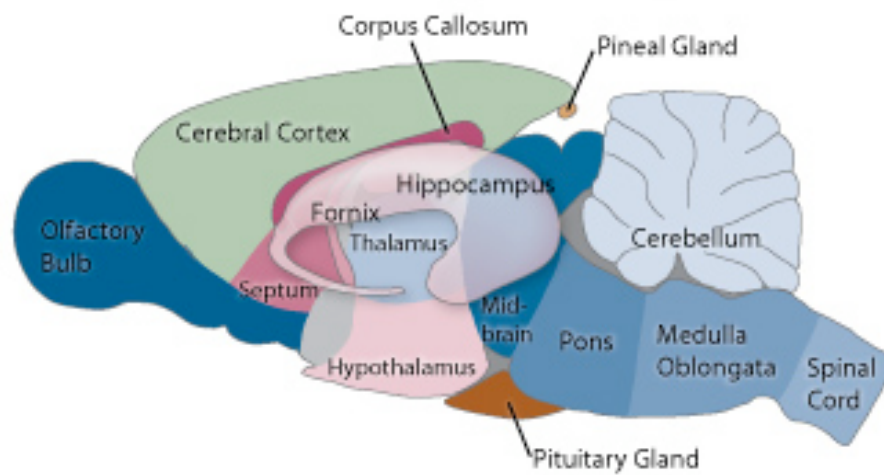
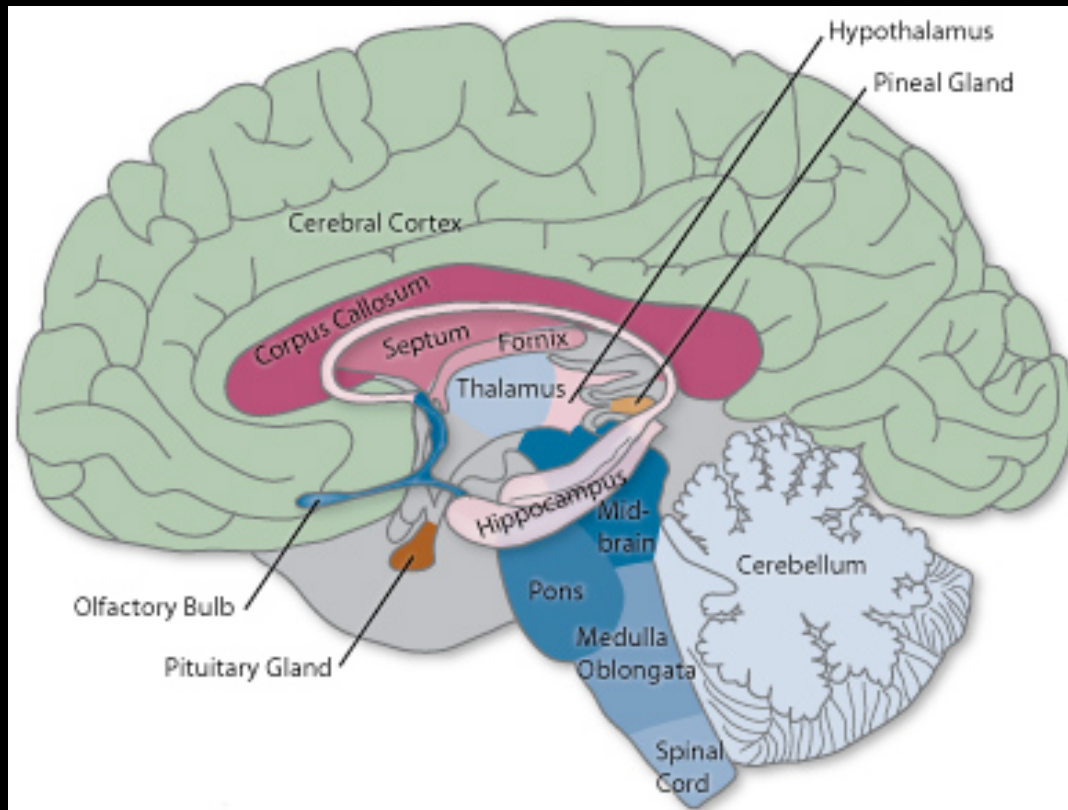
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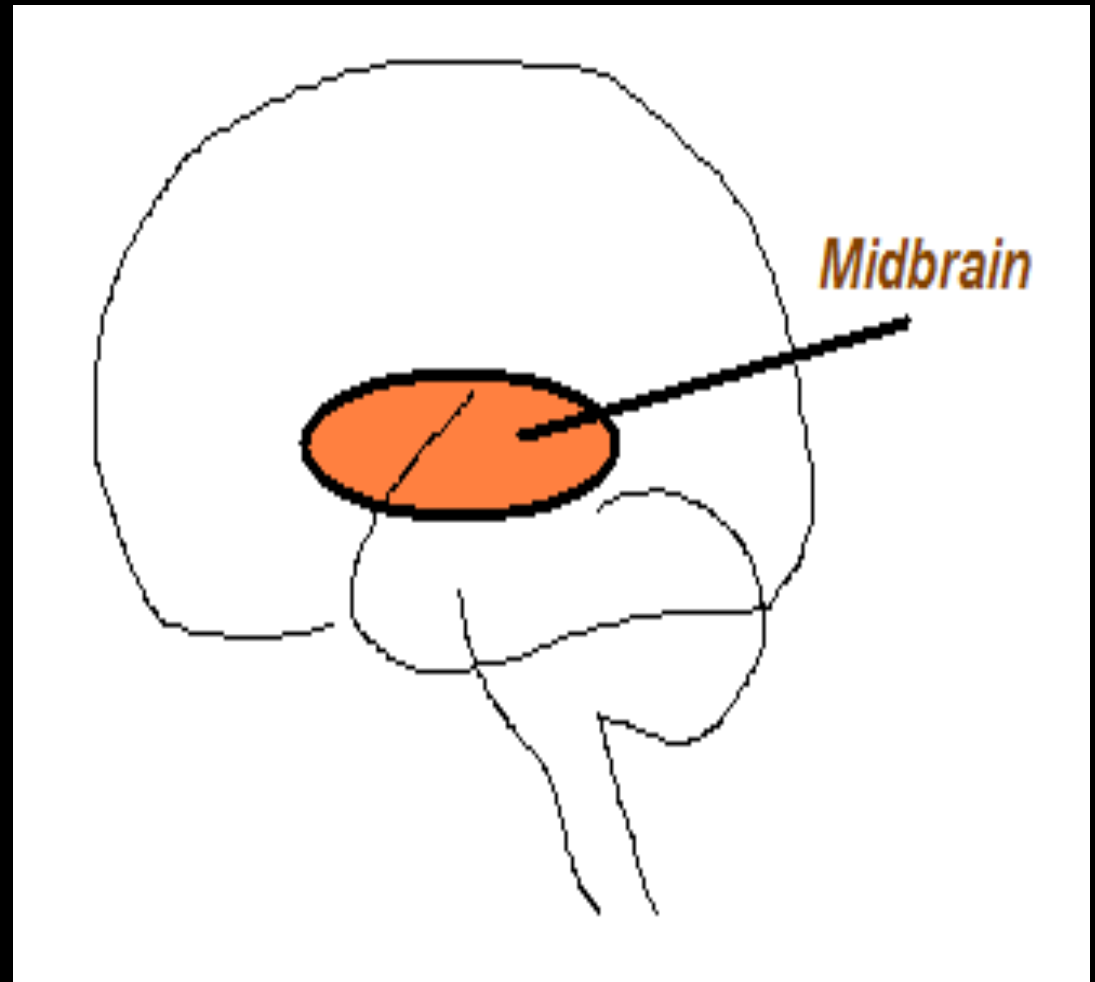
The “Reward Centers” (Pathway) of the Brain





The Limbic Brain is your **SURVIVAL** brain
It handles:

- ***EAT!***
- ***KILL! (defend)***
- ***SEX !***



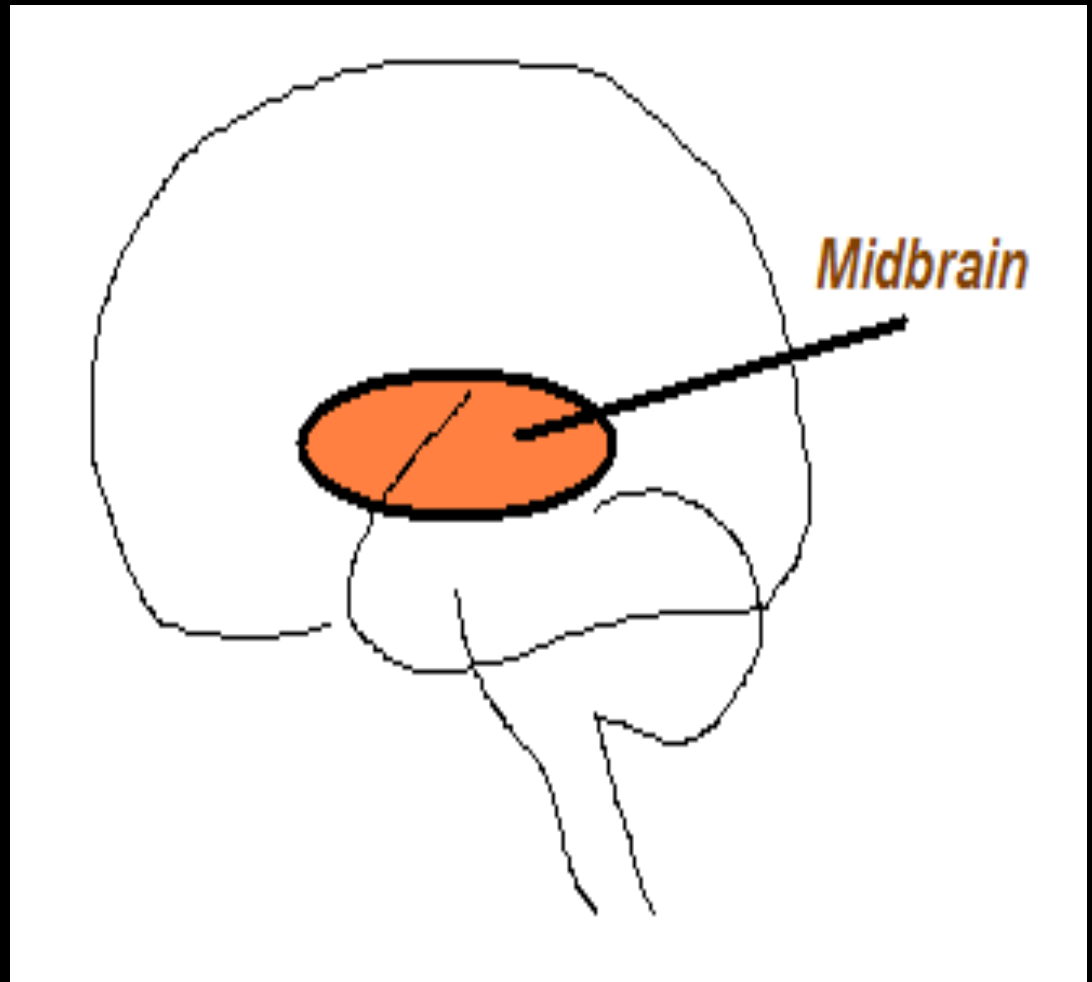
In addicted mice, the drug goes to the top of the list, “hijacking” the normal survival hierarchy

New #1: DRUG!

2. EAT!

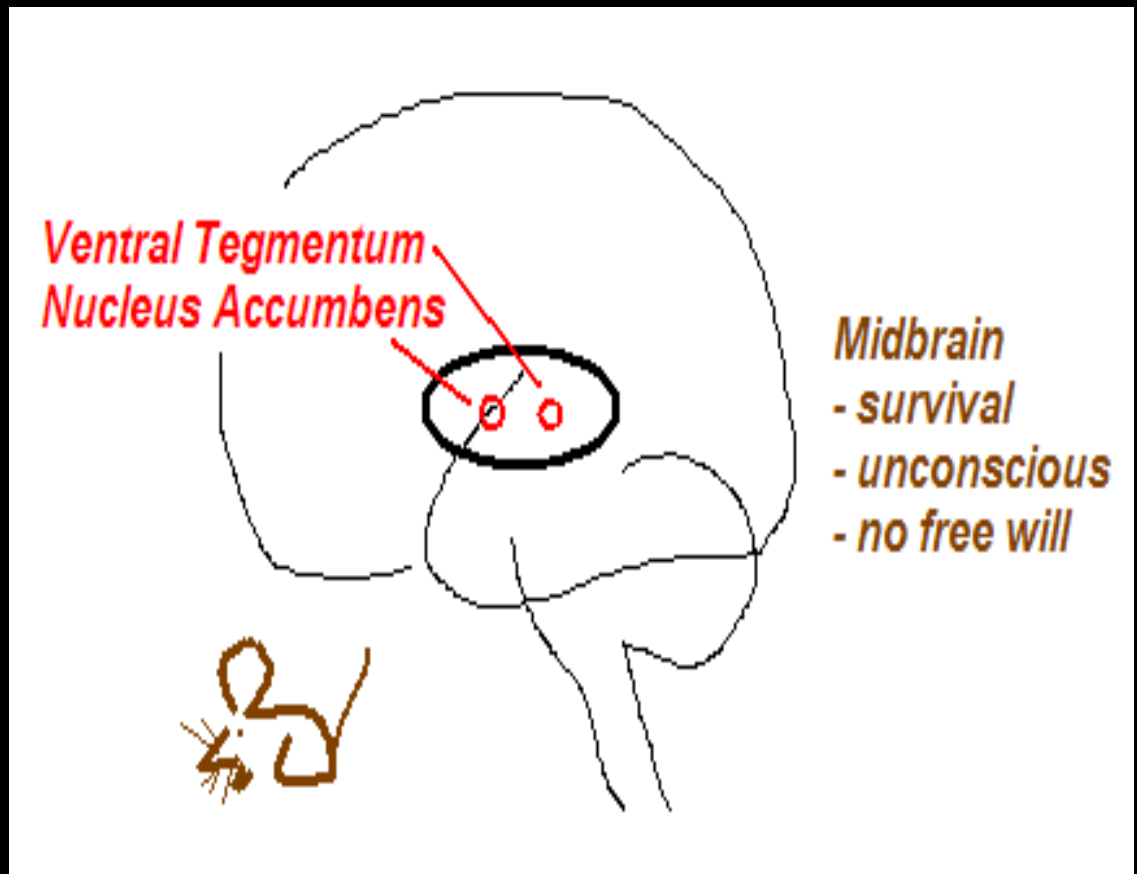
3. KILL! (defend)

4. SEX !



*Mice preferentially self-administer cocaine **ONLY** to the Reward Centers of the Midbrain*

- *To the exclusion of all other survival behaviors*
- *To the point of death*



Mice can get addicted to drugs!



Mice get addicted to drugs, but ...

- *Mice don't weigh moral consequences*
- *Mice don't consult their "Mouse God"*
- *Mice aren't sociopaths*
- *Mice don't have bad parents*
- *There are no "Mouse Gangs"*



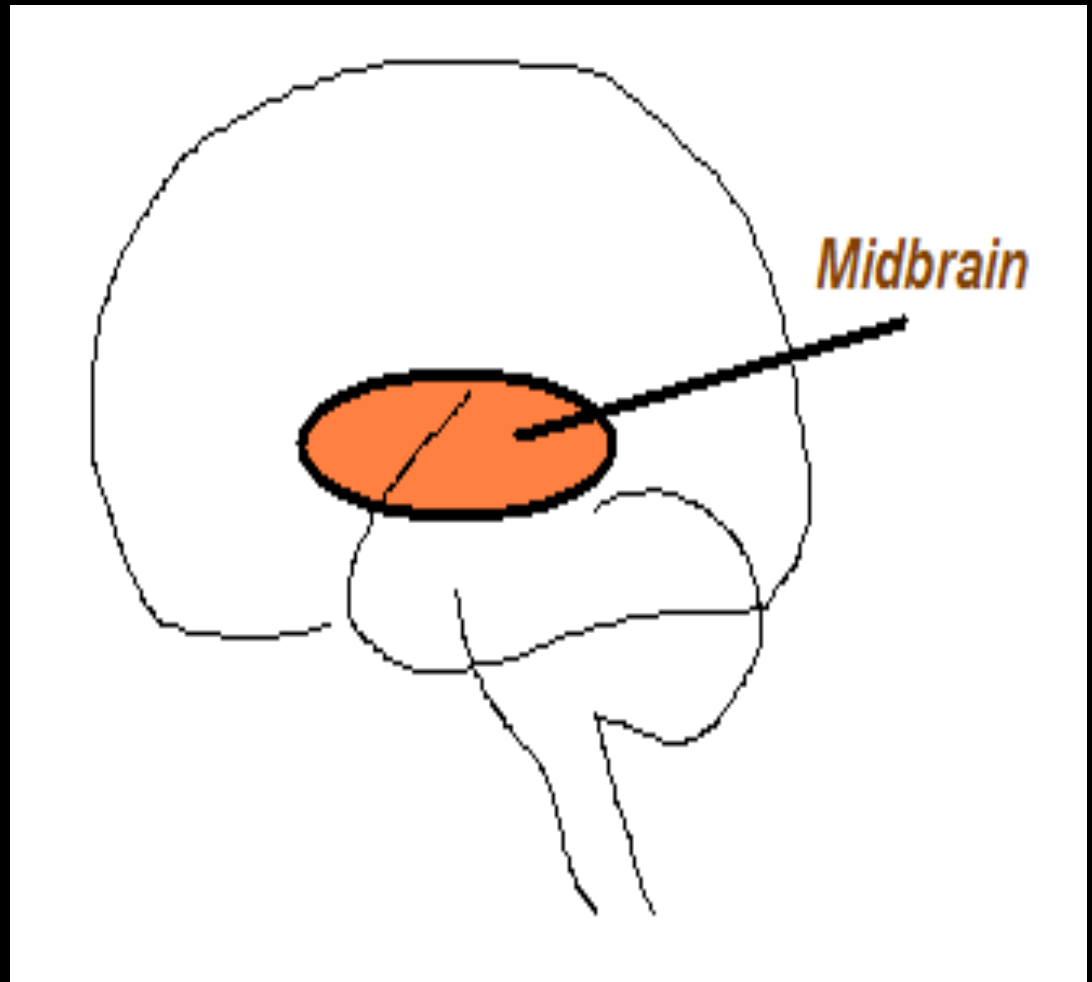
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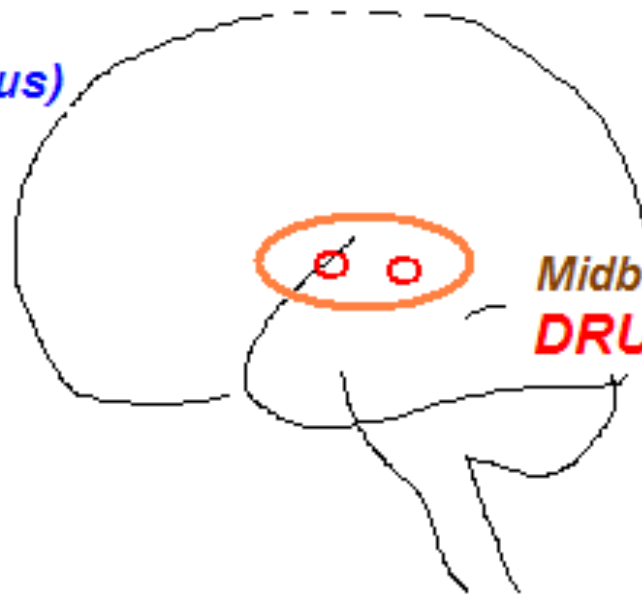
3. KILL!

4. SEX !



The Drug becomes Survival at the level of the unconscious . . .

Cortex
(conscious)



Midbrain (unconscious)

DRUG = SURVIVAL

A line is crossed ...

NON-ADDICT -----|----> ADDICT

(non-user)

(experimenter)

(user)

(abuser)

DRUG = DRUG

DRUG = SURVIVAL

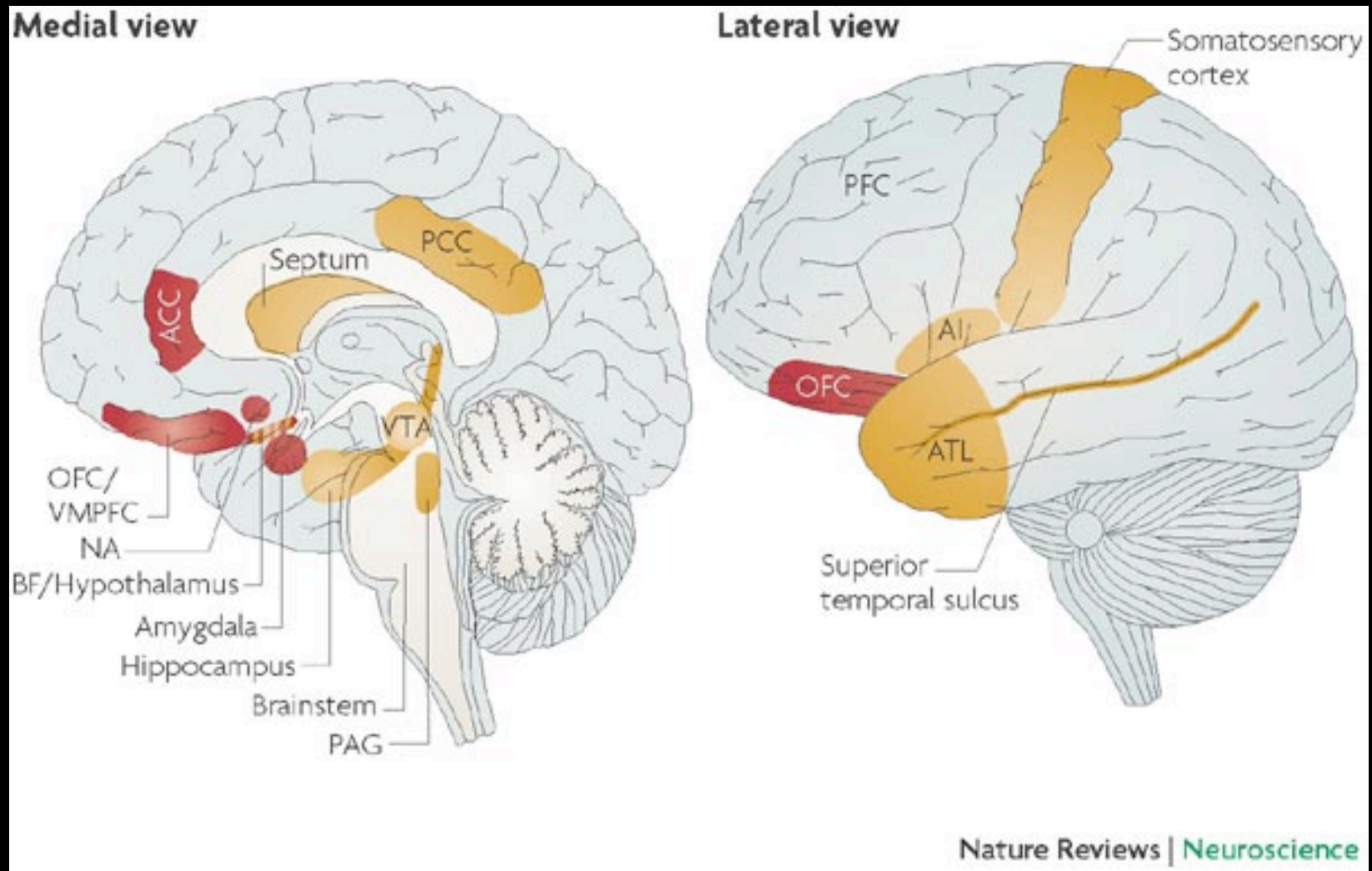
**Addiction is a disorder
of the brain's “hedonic system”**

Essentially ... it's a broken “pleasure sense”





The Key Parts of the Limbic Brain



Addiction is a disorder of ...

5.

4.

3.

2.

1. ... GENES (vulnerability)

Addiction is a disorder of ...

5.

4.

3.

2. ... REWARD

(hedonic system)

1. ... GENES

(vulnerability)

Addiction is a disorder of ...

5.

4.

3. ... **MEMORY** (learning)

2. ... **REWARD** (hedonic system)

1. ... **GENES** (vulnerability)

Addiction is a disorder of ...

5.

4. ... **STRESS** (anti-reward system)

3. ... **MEMORY** (learning)

2. ... **REWARD** (hedonic system)

1. ... **GENES** (vulnerability)

Addiction is a disorder of ...

- 5. ... CHOICE (motivation)**
- 4. ... STRESS (anti-reward system)**
- 3. ... MEMORY (learning)**
- 2. ... REWARD (hedonic system)**
- 1. ... GENES (vulnerability)**

Addiction is a disorder of ...

5.

4.

3.

2.

1. ... **GENES** (vulnerability)

Genetic Vulnerability

- Genetic difference determine “low responders” vs. “high responders” to the effects of **alcohol** (low responders more likely to become alcoholics)
- There are genetic differences in how people respond to **methylphenidate (Ritalin)** injections (some like it, some don’t care) implying different vulnerabilities
- For addicts, drugs really do “feel” different than they do to non-addicts

Addiction is a disorder of ...

5.

4.

3.

2. ... REWARD

(hedonic system)

1. ... GENES

(vulnerability)

Addiction Neurochemical #1: Dopamine

- All drugs of abuse and potential compulsive behaviors release Dopamine
- Dopamine is the first chemical in the cascade of chemicals that generate a rewarding experience
- DA is the chemical of salience (survival importance)
- DA is more about “wanting” than “liking”
- DA is more about expectation than consummation
- DA signals reward prediction error - it tells the brain when something is “better than expected”



**Model 123 with
Odyssey® Styling**







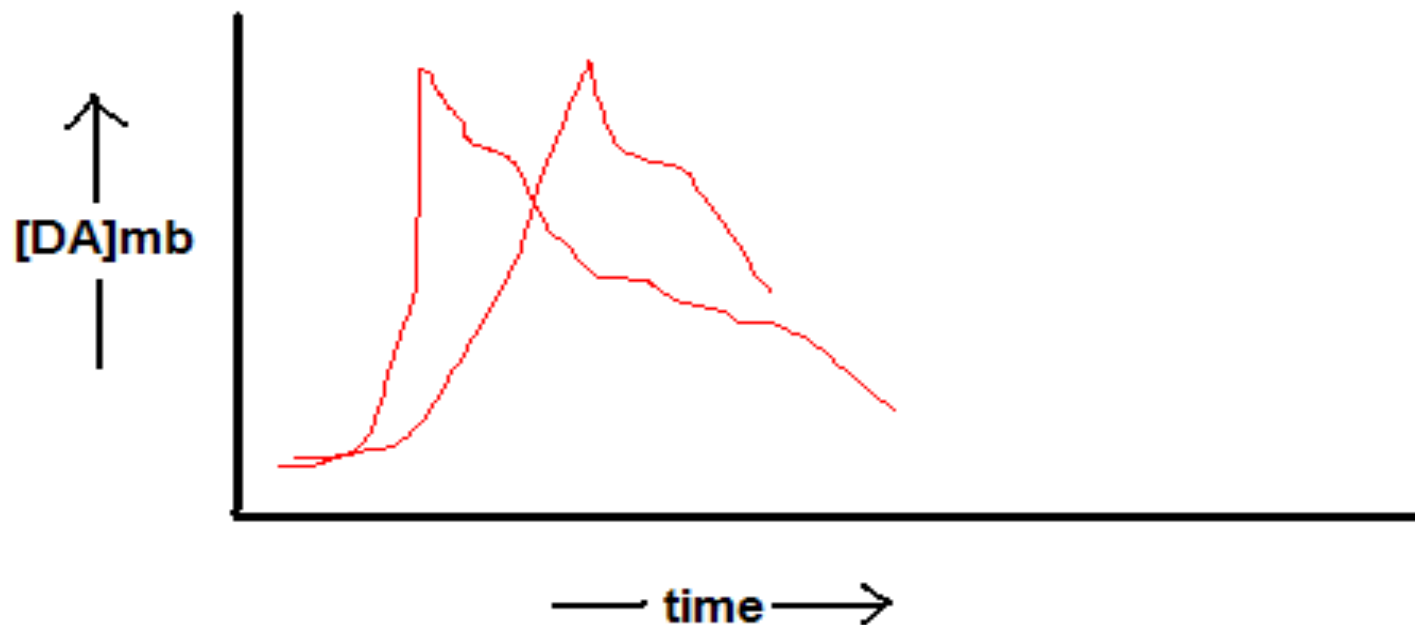
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Dopamine-Releasing Chemicals

- **Alcohol & Sedative/Hypnotics**
- **Opiates/Opioids**
- **Cocaine**
- **Amphetamines**
- **Entactogens (MDMA)**
- **Entheogens/Hallucinogens**
- **Dissociants (PCP, Ketamine)**
- **Cannabinoids**
- **Inhalants**
- **Nicotine**
- **Caffeine**
- **Anabolic-Androgenic Steroids**

Drugs cause Dopamine Surges in the midbrain reward system



Dopamine-Releasing Behaviors

- **Food (Bulimia & Binge Eating)**
- **Sex**
- **Relationships**
- **Other People**
 (“Codependency,” Control)
- **Gambling**
- **Cults**
- **Performance**
 (“Work-aholism”)
- **Collection/Accumulation**
 (“Shop-aholism”)
- **Rage/Violence**
- **Media/Entertainment**

The Full Spectrum of Addiction

- **Alcohol & Sedative/Hypnotics**
- **Opiates/Opioids**
- **Cocaine**
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 (“Shop-aholism”)
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Addiction is a disorder of ...

5.

4.

3. ... **MEMORY** (learning)

2. ... **REWARD** (hedonic system)

1. ... **GENES** (vulnerability)

Addiction Neurochemical #2: Glutamate

- The most abundant neurochemical in the brain
- Critical in memory formation & consolidation
- All drugs of abuse and many addicting behaviors effect Glutamate which preserves drug memories and creates drug cues
- And ... glutamate is the neurochemical of “motivation” (it initiates drug seeking)

The hypofrontal/craving brain state represents and imbalance between 2 brain drives

Amygdalar-Cortical Circuit

- **“GO!”**
- Impulsive
- Non-reflective
- Poorly conceived
- Socially inappropriate

THERE'S TOO MUCH OF THIS

Cortico-Striatal Circuit

- **“STOP!”**
- Organized, Attentive
- Sensitive to consequences
- Well-planned
- Socially appropriate

THERE'S TOO LITTLE OF THIS

Addiction is a disorder of ...

5.

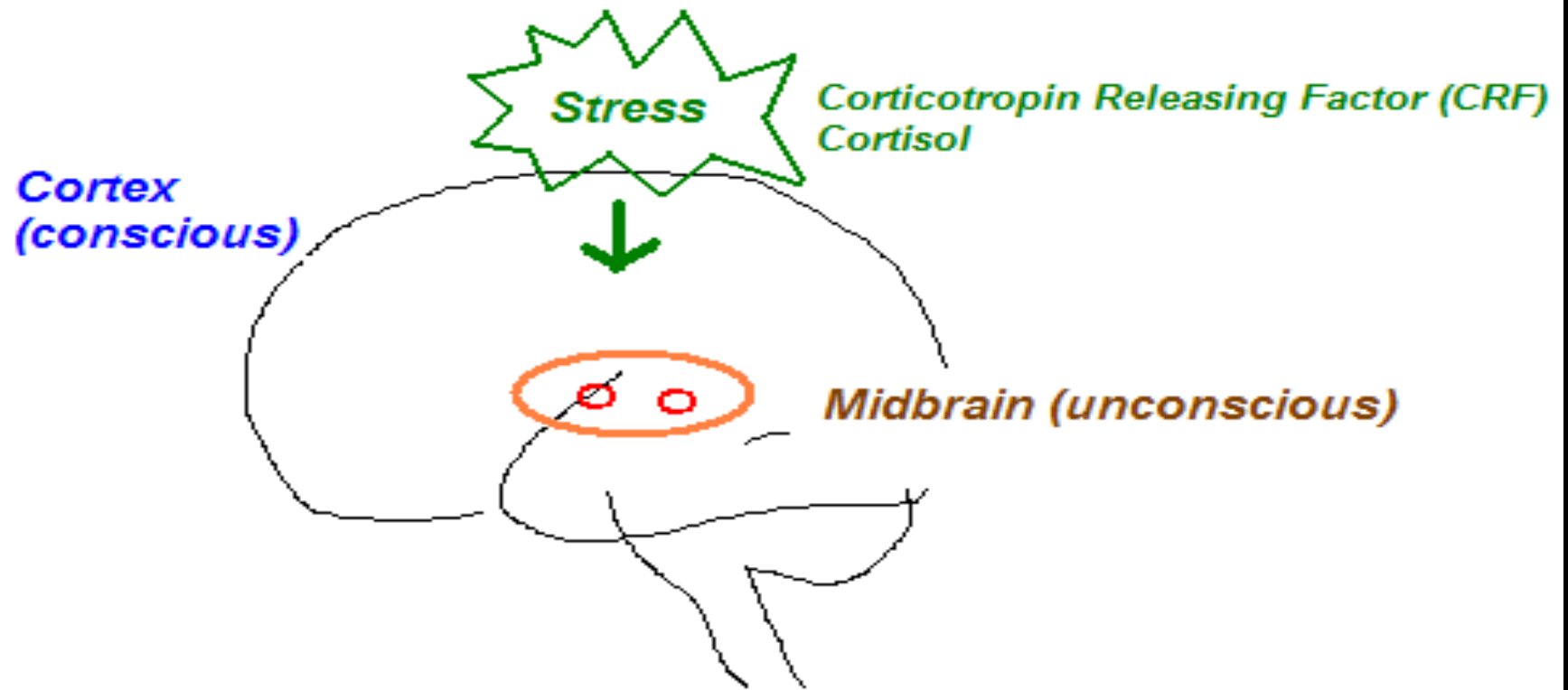
4. ... **STRESS** (anti-reward system)

3. ... **MEMORY** (learning)

2. ... **REWARD** (hedonic system)

1. ... **GENES** (vulnerability)

STRESS : a (the?) major causal agent in addiction





CHRONIC, SEVERE STRESS = \uparrow CRF

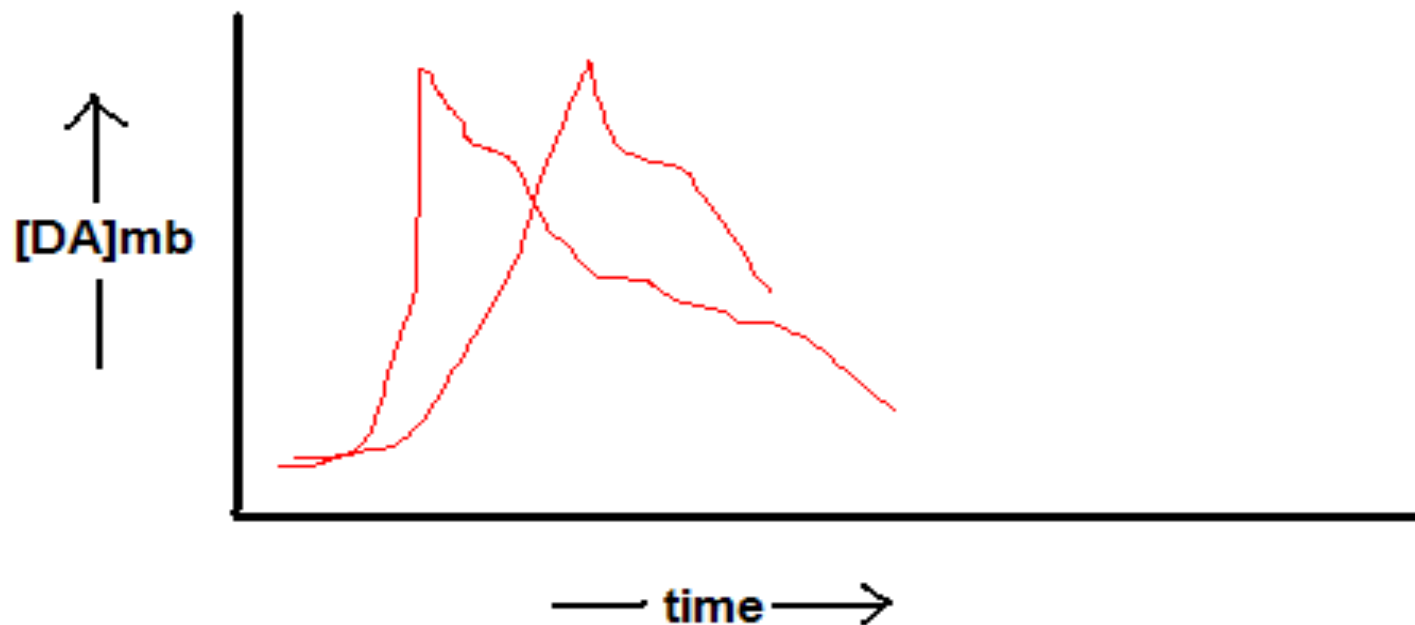
and \uparrow CRF = \downarrow DAD2 receptors

and \downarrow DAD2 receptors = Anhedonia

Anhedonia: Pleasure “deafness”

(the patient is no longer able to derive normal pleasure from those things that have been pleasurable in the past)

Drugs cause Dopamine Surges in the midbrain reward system



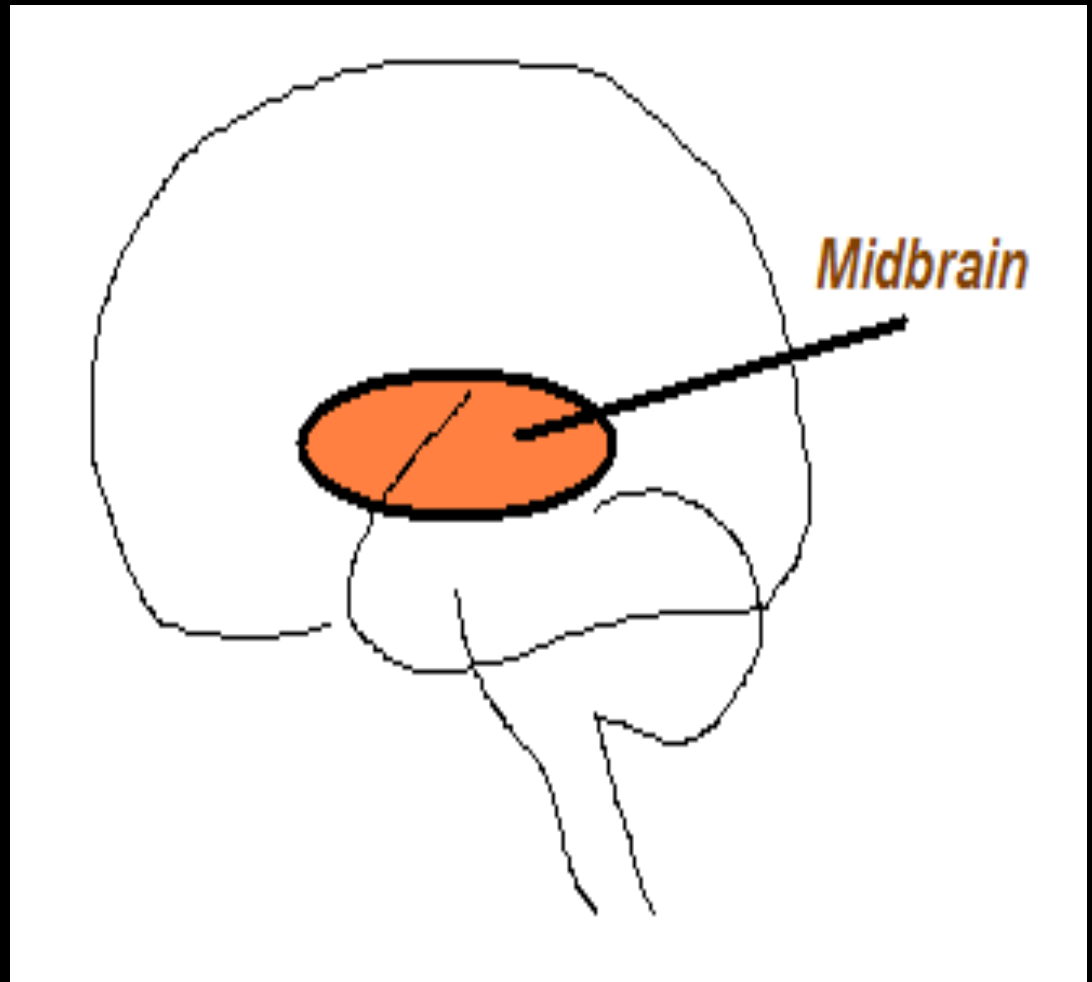
In addicted mice, the drug goes to the top of the list, “hijacking” the normal survival hierarchy

New #1: DRUG!

2. EAT!

3. KILL! (defend)

4. SEX !

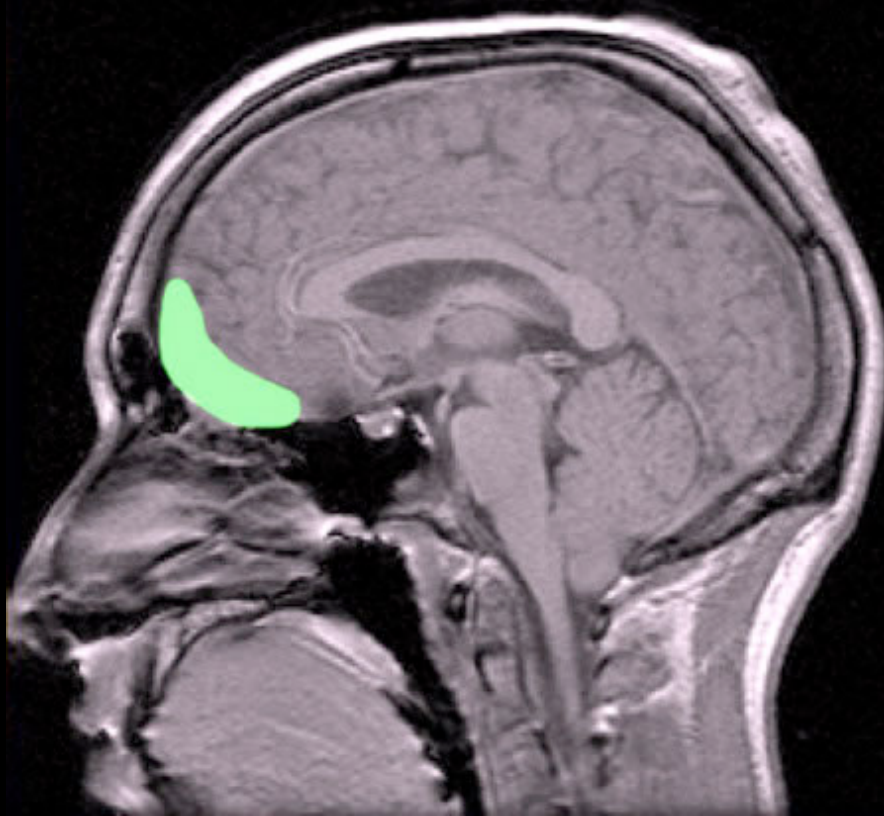


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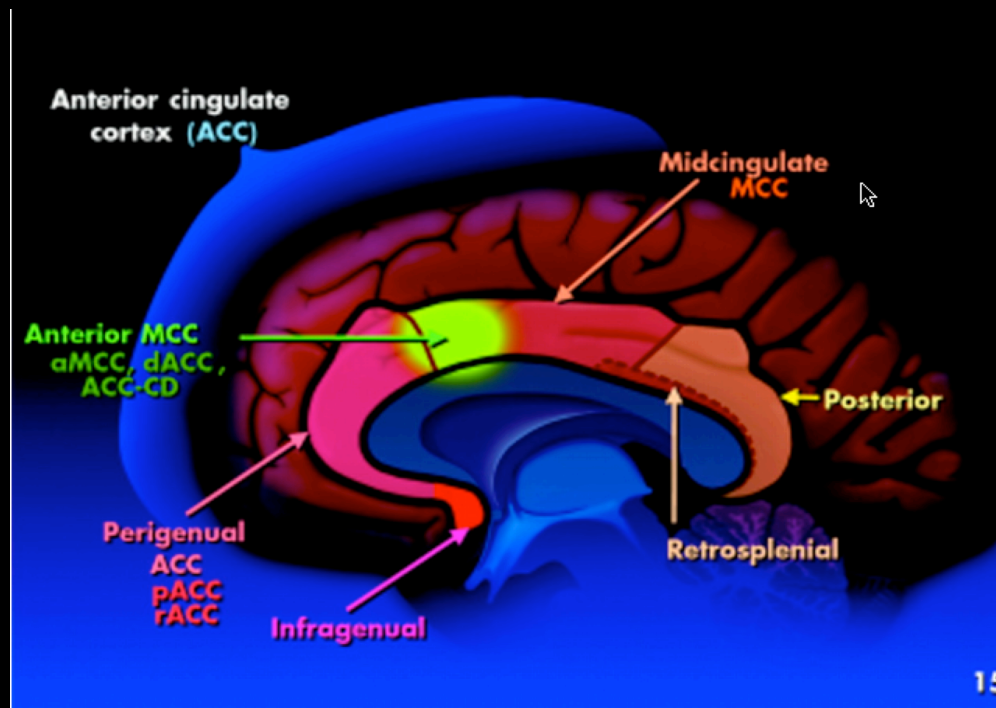


damage to Orbitofrontal Cortex (OFC)



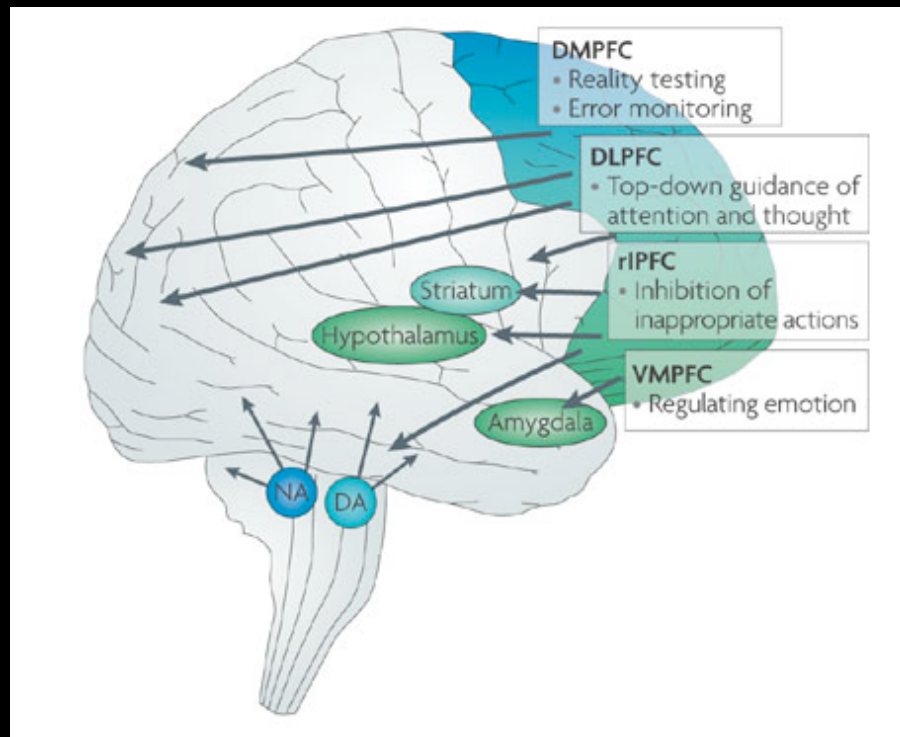
- Causes a loss of a crucial behavioral guidance system
- Responses are impulsive and inappropriate
- Deficits of self-regulation
- Inability to properly assign value to rewards (such as money vs. drugs)
- Tendency to choose small & immediate rewards over larger but delayed rewards

damage to Anterior Cingulate Cortex (ACC)



- Just as with OFC damage: causes a loss of a crucial behavioral guidance system
- Inflexibility/Inability to respond to errors in the past with regard to rewards/punishments
- Deficits in social responding due to decreased awareness of social cues

damage to Prefrontal Cortex (PFC)



- Failure of executive function

Hypofrontality

- Bechara: research on pts with vmPFC & OFC lesions
- “Myopia for the future” - cognitive impulsiveness
 - these patients prefer immediate but disadvantageous rewards over rewards that are delayed but advantageous in the long run
 - their decisions are guided primarily by immediate prospects and are insensitive to positive or negative future consequences (rewards or punishments)
 - they deny or are unaware of their problem
- Scans of vmPFC patients are similar to Sub Abuse pts

Why the “Choice” argument fails ...

- It fails to take into account ***CRAVING***
- The addict cannot choose to not ***crave***
- It measures addiction only by the addict's external ***behavior***
- It ignores the ***suffering*** of the patient

*So ... how DO we break the hold
of craving and turn the Frontal
Cortex back “on” ?*

ASAM Addiction Definition (Aug 2011)

A primary, chronic and relapsing brain disease
of reward (nucleus accumbens),
memory (hippocampus & amygdala),
motivation and related circuitry (ACC, basal forebrain)
that alters motivational hierarchies such that addictive
behaviors supplant healthy, self-care behaviors

If Addiction is a “Disease,” then ...

- *Addicts are patients!*
- *Addicts have the same rights as all patients*
- *All the ethical principles that apply to other patients now also apply to addicts*
- ***Addiction has parity***

Questions?

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Please also see: www.addictiondoctor.com

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